A DISSERTATION

ON

STUDY OF SERUM URIC ACID LEVELS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND ITS CORRELATION WITH THE SEVERITY ASSESSED BY KILLIP CLASSIFICATION AND 2D ECHOCARDIOGRAM

Submitted to

THE TAMILNADU DR. M. G. R. UNIVERSITY
CHENNAI

In partial fulfillment of the regulations
for the award of

M. D. DEGREE IN GENERAL MEDICINE
BRANCH I

GOVERNMENT MOHAN KUMARAMANGALAM
MEDICAL COLLEGE, SALEM
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Government Mohan Kumaramangalam Medical College Hospital

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled "**STUDY OF SERUM URIC ACID LEVELS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION AND ITS CORRELATION WITH THE SEVERITY ASSESSED BY KILLIP CLASSIFICATION AND 2D ECHOCARDIOGRAM"** is a bonafide and genuine research work carried out by me under the guidance of ***Dr. S. R. SUBRAMANIAN, M. D. D.Ch,*** **Professor & Head of the Department**, Department of General Medicine and under the co guidance of ***Dr. P. KANNAN , M. D., D.M. (Cardio), Professor and Head of the Department*** of Cardiology, Government Mohan Kumaramangalam Medical College Hospital, Salem, Tamil Nadu, India.

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LIST OF ABBREVIATIONS

ACC	-	American College of Cardiology
ACS	-	Acute Coronary Syndrome
AKI	-	Acute Kidney Injury
AMI	-	Acute Myocardial Infarction
APACHE	-	Acute Physiology Score And Chronic Health Evaluation
ARIC	-	Atherosclerosis Risk In Communities
		Electrocardiogram
ASMI	-	Anteroseptal Myocardial Infarction
AWMI	-	Anterior Wall Myocardial Infarction
BMI	-	Body Mass Index
BNP	-	Brain Natriuretic Peptide
CAD	-	Coronary Artery Disease
CABG	-	Coronary Artery Bypass Graft
CVD	-	Cardiovascular Disease
DM	-	Diabetes mellitus
ECG	-	Electrocardiograph
e NOS	-	Endothelial Nitric Oxide Synthase

GISSI	-	Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardio
GRACE	-	Global Registry of Acute Coronary Events
Hs-CRP	-	High sensitive C Reactive Protein
HT	-	Hypertension
IHD	-	Ischemic Heart Disease
IL-6	-	Interleukin 6
IWMI	-	Inferior Wall Myocardial Infarction
LBBB	-	Left Bundle Branch Block
LDL	-	Low Density Lipoprotein
LDL	-	Small dense oxidized LDL
Lp(a)	-	Lipoprotein a
LV	-	Left Ventricle
MACE	-	Major Adverse Cardiac Events
MET	-	Metabolic equivalent
MI	-	Myocardial Infarction
MPO	-	Myeloperoxidase
MONICA	-	Monitoring Trends and Determinants in Cardiovascular Disease
NO	-	Nitric Oxide
NRMI	-	National Registry Of Myocardial Infarction

NSTEMI	-	Non ST Elevation Myocardial Infarction
PCI	-	Percutaneous Coronary Intervention
RHD	-	Rheumatic Heart Disease
ROS	-	Reactive Oxygen Species
S ICAM1	-	Soluble Intercellular Adhesion Molecule-1
STEMI	-	ST Elevation Myocardial Infarction
SUA	-	Serum Uric Acid
TGL	-	Triglyceride
TIMI	-	Thrombolysis In Myocardial Infarction
UA	-	Unstable Angina
URAT1	-	Urate Anion Exchanger 1
VF	-	Ventricular Fibrillation
VSR	-	Ventricular Septal Rupture
VT	-	Ventricular Tachycardia
XOR	-	Xanthine Oxidoreductase

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Ethical Committee Meeting held on 18.06.2015 at 10.00 A.M in the Seminar Hall, IInd Floor, Medicine Block, Govt. Mohan Kumaramangalam Medical College Hospital, Salem - 01.

The following Members were attended the Meeting.

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1.	Dr. M.C. Vasif Mayan, II Year, Post Graduate Student of MD (General Medicine), GMKMC, Salem-30.	"Study of serum uric acid levels in patients with acute myocardial infarction and its correlation with the severity assessed by killips classification and 2-D Echocardiogram".	Dr. S.R. Subramanian, MD., Professor and HOD of General Medicine , GMKMC, Salem-30.	Approved

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INTRODUCTION

Myocardial Infarction is one of the key components of cardiovascular disease burden all around the world. Coronary heart disease constitutes an immense public health problem.[1] Coronary heart disease mortality has now decreased over the years, but the huge burden of its associated complications is on the rise. Effective utilization of multifaceted approaches (like drug discovery, clinical trials, and clinical policies) are necessary to reduce cardiac disease burden along with proper identification of patients with cardiovascular events, and also the incidence and outcome of such disease. The epidemiology of Myocardial Infarction plays an immense role in proper investigation of such cardiovascular disease burden.[2]

Majority of deaths from cardiac events, including coronary vascular disease and cerebro-vascular accidents occur in developing countries. Coronary artery disease has achieved epidemic proportion in India. Comparing the Indian subcontinent with other countries, coronary artery disease related mortality is still high with cardiac disease manifesting 10 years earlier than the rest of the world. The huge burden in Indian subcontinent may be attributed to its large population and high prevalence of cardiovascular risk factors which has emerged as a part of urbanization. As per the current scenario, cardiovascular death accounts for about

50% of total death, and it is predicted that, it may go up to 2/3rd of total death by 2020.[3]

Considering this huge burden in our part of the world, it would be very helpful if a simple, common, biochemical investigation can act as prognostic predictor in those admitted with cardiac illness.

Multiple molecules have been studied and used as prognostic predictors in Acute Myocardial Infarction. Purine metabolism results in the production of Uric Acid. Serum levels of uric acid is influenced by multiple factors like production and elimination rates, race, demography, diet, habituations, organ failure and medications.[4,5] On the molecular level, uric acid acts an antioxidant, and can result in the dysfunction of endothelial cells, proliferation of vascular smooth muscles and aggregation of platelets on vessel walls resulting in micro inflammation and tubulo-interstitial inflammation. Increased serum uric acid has been associated with increased incidence of metabolic syndrome, chronic kidney diseases, diabetes mellitus and cerebro-vascular accidents, proving uric acid as an important secondary marker of cardiovascular disease on the basis of pathophysiological and etiological processes, according to some researchers.[6] Another important factor supporting the use of Uric acid as a prognostic indicator of Myocardial infarction is that it is cheap to be tested.

Keeping all this in mind and the idea that uric acid can be used as an important yet independent prognostic predictor for worse outcomes, it would be helpful for earlier and accurate assessment of Acute Myocardial Infarction going in for deterioration and for implementation of more effective and timely therapeutic strategies.

AIMS and OBJECTIVES

1. To estimate the serum Uric acid levels in patients with acute myocardial infarction.
2. To correlate the levels of serum uric acid with the severity of myocardial infarction as assessed by the Killip Classification, TIMI score and GRACE score.
3. To correlate the levels of serum Uric acid with the two dimensional echocardiographic findings.

REVIEW OF LITERATURE

HISTORY

In the Central and Eastern parts of Europe, autopsies revealed atherosclerotic lesions that involved coronary arteries, based on studies by Adam Christian Thebesius - a well-known physician, who then used the term 'ossification of coronary arteries for the atherosclerotic lesions'.

Fig 1 Adam Christian Thebesius

Giovanni B. Morgagni (1682-1771) who published his work, a collection of case reports in 1761 mentioned the symptomatology of angina pectoris and autopsy protocol showing ossification of aorta and its branches in such patients. Nicolas Rougnon deMagny (1727-1799) of France made the discovery of ischemic heart disease. Dr. William Heberden (1710-1801) also contributed to it.

Fig: Giovanni B. Morgagni ; *Dr. WIliam Heberden ;* *Nicolas Rougnon de Magny*

(Figure - 2)

Vilnius Jozef Chrzezonowicz, Jan Cenner and Andrzej Janikowski described 'angina pectoris'. All of them were of polish origin. First described case of a coronary embolism was by an Austrian physician, Adam Hummer in 1878, but it took nine years from that time to publish a paper regarding coronary artery embolism by another Polish physician Professor Edward-Sas-Korczynski (1844-1905). The concept of myocardial infarction, the pathological change associated with angina pectoris was suggested by Jozef Pawinski, father of Polish cardiology.

Fig: Jozef Pawinski

(Figure – 3)

In the early 20th century, clinical diagnostic era found out its basis through the discovery of electrocardiogram by William Einthoven (in 1903). Further detailing on myocardial infarction like complete occlusion or clogging of main coronary arteries were mentioned in the works of Zdzislaw Dmochowski and Walery Jaworski of Poland.

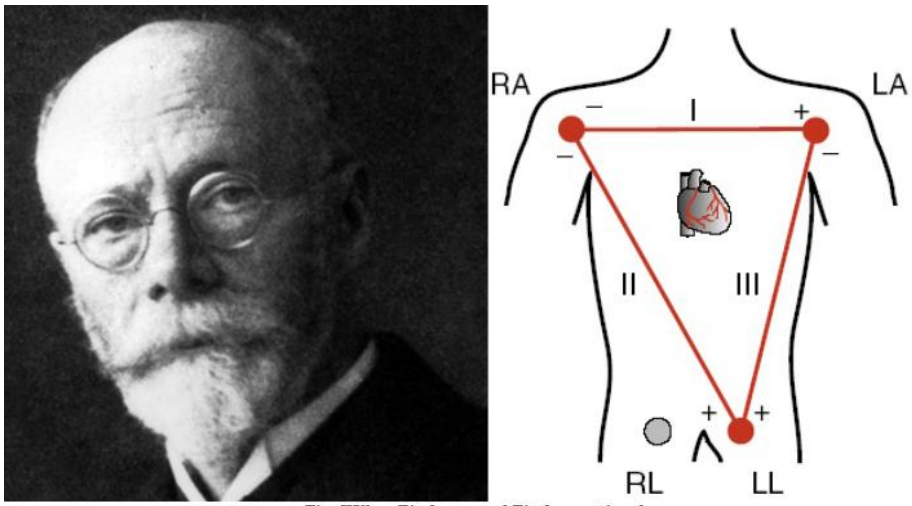


Fig: Willem Einthoven and Einthoven triangle

(Figure – 4)

The pioneers that built the backbone of the world of cardiology, thus can be inferred as the Polish Physicians.[7]

Uric acid was discovered in 1776 by Carl Wilhelm Scheeleas a constituent of bladder stone hence he named it 'uric acid' or 'bladder stone acid'. Uric acid was synthesized by Iwan Horbaczewski in the 1880s for the first time, by fusing glycine with urea by heating 3,3,3- tri-chloro-acetic acid. Though eighteenth century literature described uric acid, complete description of properties and

synthesis was achieved in 20th century. Uric acid is a yellowish white, tasteless, odourless substance in crystal or powder form, used for the commercial preparation of allantoin, alloxan, alloxautine, parabnic acid.[8]

Fig: Carl Wilhelm Scheele ; Iwan Horbaczewski

(Figure – 5)

ATHEROSCLEROSIS

Arteriosclerosis the term means "hardening of the arteries". It is basically a common term for the thickening of the walls of arteries and thus loss of its elasticity. ***Atherosclerosis***, is a Greek word rooted from words meaning "gruel" and "hardening".

An atheromatous plaque consists of a raised lesion with a soft nucleus of lipid like cholesterol and its esters covered by a fibrous cap (Fig - 6). These plaques obstructs blood flow through these vessels, or it can rupture which will in turn lead to catastrophic events like obstructive vascular thrombosis, eventually leading to ischemic injury of the vessel walls.

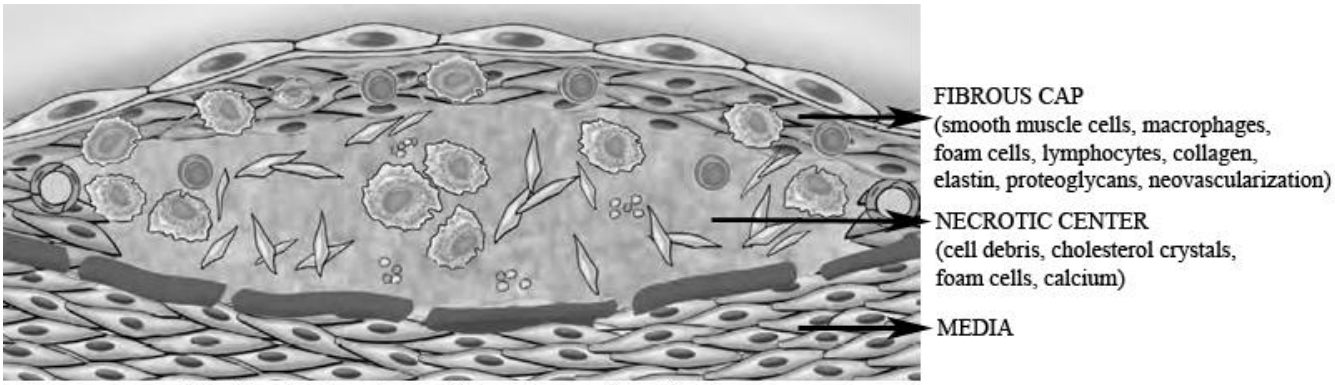


Fig: Basic structure of an atherosclerotic plaque

(Figure – 6 showing basic structure of an atherosclerotic plaque)

ACUTE MYOCARDIAL INFARCTION

DEFINITION

"The term Acute Myocardial infarction should be used when there is evidence of myocardial necrosis in a clinical setting constituent with acute myocardial ischaemia".

Criteria essential for the diagnosis of MYOCARDIAL INFARCTION.

- *Detection of rise and/or fall of cardiac biomarker values (preferably troponin T)* with at least one value above 99th reference limit and

With atleast one of the following.

1. Symptoms of ischemia
2. New or presumed new significant ST segment T wave changes or new left bundle branch block.
3. Development of pathological 'Q' waves in ECG.
4. Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality.
5. Identification of an intracoronary thrombus by angiography or autopsy.

- Cardiac death with symptoms suggestive of myocardial ischemia, presumed new ECG changes or new LBBB, but death occurred before biomarkers were obtained, or before their values would be increased.
- Percutaneous coronary intervention related MI is defined by elevation in Troponin values or >20% rise from baseline values.

In addition,

1. Symptoms of ischemia
2. ECG changes
3. Angiographic findings consistent with a procedural complication
4. Imaging demonstration of loss viable myocardium.

- Stent thrombosis associated with MI when detected by angiography or autopsy with a rise in cardiac biomarker above the 99th percentile.
- CABG related MI defined by elevation of cardiac biomarker, normal baseline values with either ECG changes, angiographic documented new graft or new native coronary artery occlusion, or imaging evidence.

Criteria for prior myocardial infarction

1. Pathological Q wave with or without symptoms in the absence of non-ischemic causes.
2. Imaging evidence of regional loss of viable myocardium that is thin and fails to contract in the absence of non-ischemic causes.
3. Pathological findings of a prior MI.

Table – 1 : Criteria for prior MI (any one)[9]

Types of Myocardial Infarction

TYPES OF MYOCARDIAL INFARCTION
Type 1 - Spontaneous myocardial infarction
Type 2 - Myocardial infarction secondary to ischemic imbalance
Type 3 - Myocardial infarction resulting in death when biomarker values are unavailable.
Type 4a - Myocardial infarction related to percutaneous coronary intervention
Type 4b - Myocardial infarction related to stent thrombosis
Type 5 - Myocardial infarction related to CABG.

Table - 2 : Third Universal Definition of types of MI[9]

EPIDEMIOLOGY

Several well established studies conduct heart disease surveillance to provide epidemiological data on myocardial infarction, names of which are described below. (Table – 3)

Minnesota Heart survey
Atherosclerosis risk in communities (ARIC)
Olmsted county study
Worcester Heart Attack Study
Framingham heart study
Corpus Christi Heart project
WHO MONICA project (Multinational Monitoring of trends and determinant in Cardiovascular disease)
Population registries like FINAMI, NRMI & GRACE.

Table – 3 studies providing epidemiological data on MI

As a result of secondary prevention and adequate medical treatment, the coronary mortality rate has reduced and shows stable incidence trends.[2] In the year 2003 in India, the village areas counted a CHD prevalence of 3-4% while urban areas showed 8-10%. 52% of the cardiovascular deaths occur under the age of 70 years, which implies a marked reduction in country's working population, expected to be about 17.9 million years by 2030. Urbanization led to the intake of energy dense foods, decrease in physical

activity, increased psychosocial stress which promoted dysglycemia, hypertension and dyslipidemia, which are all risk factors for cardiovascular disease. This epidemic of coronary artery disease warrants urgent action like expanding public education, control of primordial and primary risk factors by population based interventions and effective preventive strategies.[4]

The key results of South Asian components of the INTER-HEART study, a study based on reports from 52 countries all around the world, including India were,

1. Average life span of patients with Acute Coronary Artery Disease in South-Asian countries is 5-10 years lesser than western countries.
2. Comparison of gender differences in Acute Myocardial infarction showed that males have 5-6 years lesser life span than females.
3. Increased number of risk factors explains increased risk (86%) of Acute Myocardial Infarction.
4. Abnormal Apo-B/Apo-A1 ratio and smoking increases the incidence of Acute Myocardial Infarction.
5. Increased prevalence of AMI with Lower educational status.
6. Alcohol consumption on a daily basis creates negative prognosis for Acute Myocardial Infarction.[10]

The inclusion criteria of this INTER-HEART study takes into account both types of MI, NSTEMI (Non-ST segment elevation myocardial infarction) and STEMI (ST segment elevation myocardial infarction).

APPROACH TO ACUTE CORONARY SYNDROME

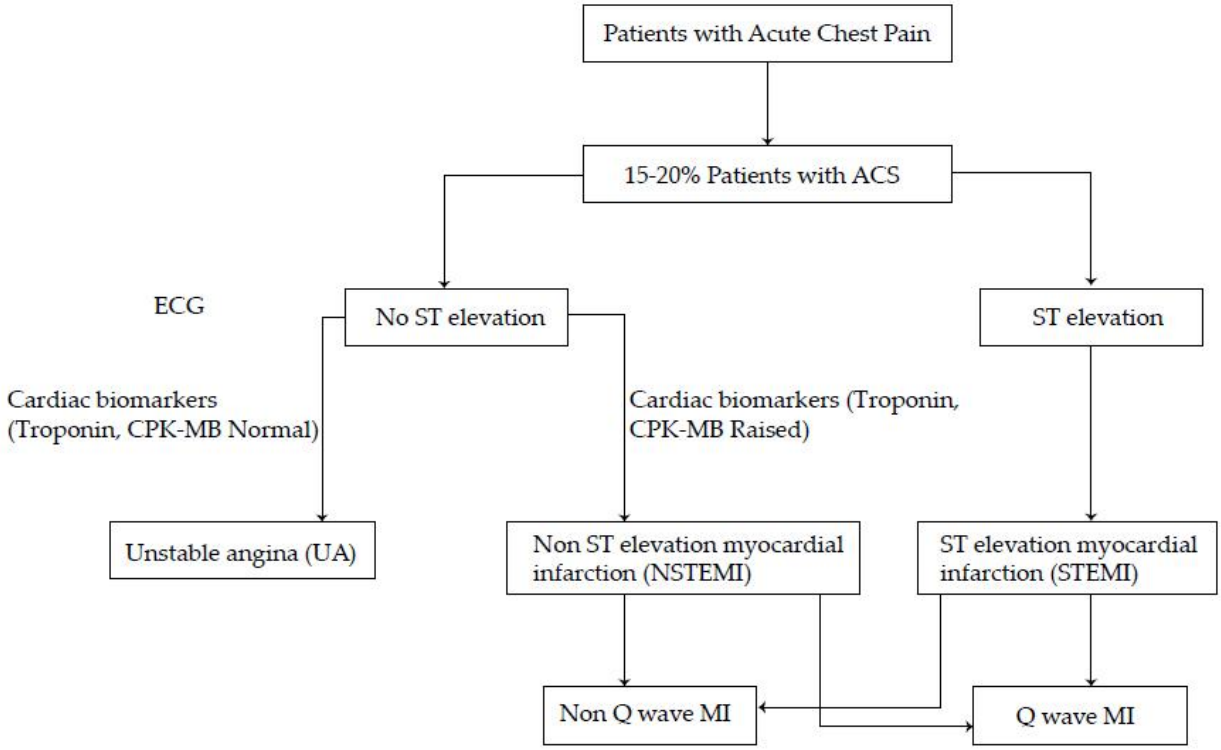


Figure – 7: Approach to ACS

NON- ST ELEVATION MYOCARDIAL INFARCTION (NSTEMI)

Patho-physiology

Four processes which are responsible for Unstable Angina or Non-ST elevation MI,

(1) Non-occlusive thrombosis superimposed on erosion, with NSTEMI caused by plaque rupture

(2) Dynamic obstruction like coronary spasm of Prinzmetal's angina.

(3) Progressive mechanical obstruction by advancing atherosclerosis or re-stenosis after percutaneous coronary intervention.

(4) Situations demanding increased supply of Oxygen to Myocardium, as in tachycardia, anemia etc...

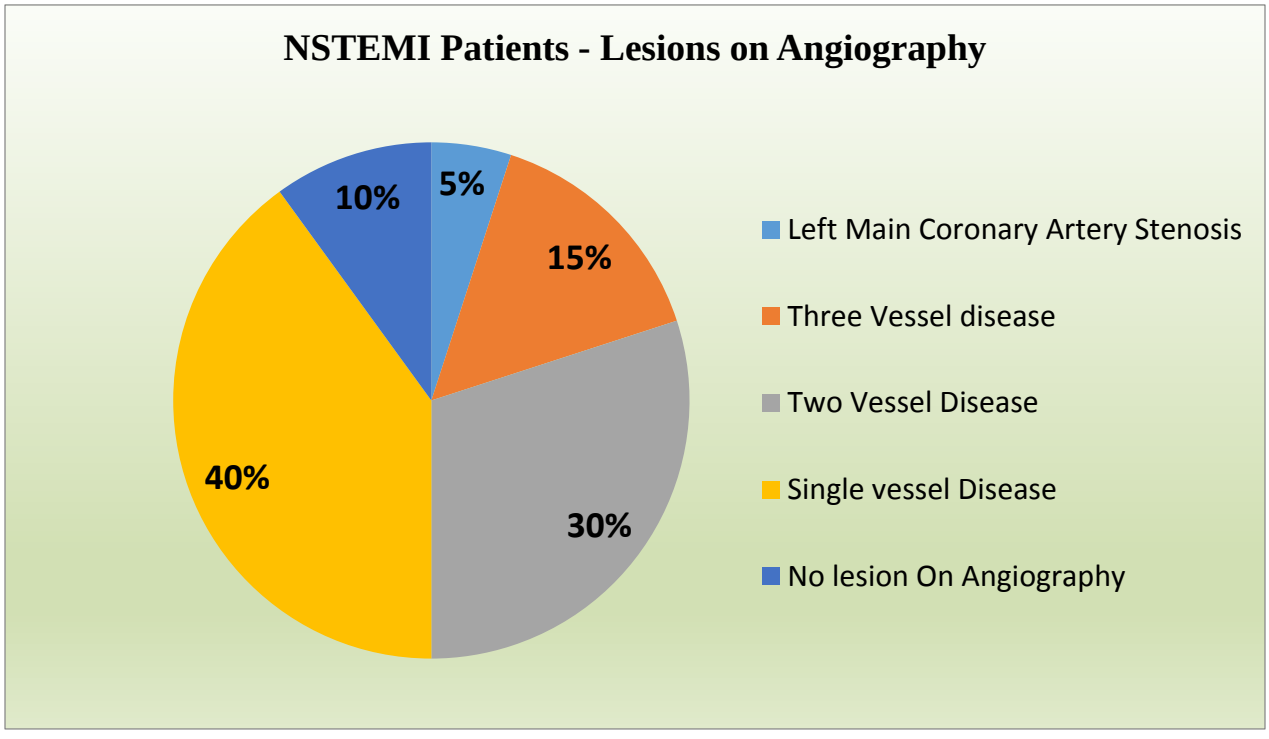


Figure - 8: Lesions on Angiography – in NSTEMI

Angioscopy revealed thrombi, rich in platelet instead of thrombi rich in fibrin & cells like that seen in STEMI.

Clinical Features

Symptoms are sub-sternal or epigastric pain with radiation to neck, shoulder, arm, or angina/equivalents such as dyspnea or epigastric discomfort. Physical examination may reveal features of atherosclerosis, evidence of peripheral artery disease, anemia, thyroid disease and transient left ventricular failure.

Investigations

1. **Electrocardiogram**

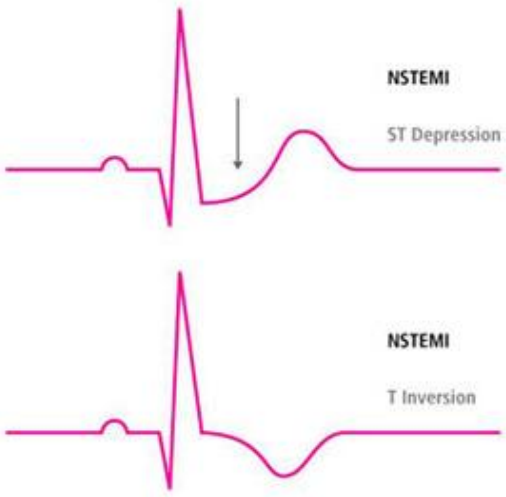


Figure 9: ECG Changes in NSTEMI

T wave inversion $\geq$ 0.3 mV

ST segment depression

Transient ST elevation

2. **Cardiac Biomarkers**

CK-MB or Troponin will be elevated.

The four major diagnostic tools are clinical history, ECG, Cardiac biomarkers and Stress testing or Coronary Imaging.

Risk factor & Prognosis

1-10% of patient with NSTEMI go in for early death (30 days), 3.5% for recurrent infarction. The thrombolysis in Myocardial Infarction Scoring system identified seven independent risk factors.

The Seven risk factors are:

1. Age $\geq$ 65 years

2. 3 or more CAD risk factors

3. Documented CAD at catheterization

4. Development of NSTEMI when patient is on Aspirin

5. Anginal episodes, more than 2 in the preceding 24 hours

6. ST segment elevation $\geq$ 0.5 mm

7. Increased levels of Cardiac biomarkers

Other factors causing increased risk of CAD are

1. T_2DM,
2. LVH,

3. Acute renal failure,
4. Increased CRP and BNP

   (CRP – C-Reactive Peptide, BNP - brain natriuretic peptide)

Treatment

Medical treatment includes Nitrates, β-blockers or Calcium Channel Blockers, Antithrombotic therapy. CURE trial demonstrating 20% relative reduction in mortality with 1% increased risk of bleeding with double antiplatelet therapy.

TRITON - TIMI 38 trial favored prasugrel as it can reduce the risk of cardiovascular death or stroke by 19% and stent thrombosis by 52% compare to clopidogrel. Heparins either unfractionated or low molecular weight remains the mainstay of therapy.

Early Invasive Strategy - Class I - Indications (in high risk patients) are

1. Recurrent angina at rest, despite treatment
2. Elevated Troponin-T or Troponin-I
3. New ST segment depression
4. Symptoms of heart failure, mitral regurgitation
5. Positive stress test
6. Ejection fraction < 40%
7. Decreased BP

8. Sustained Ventricular Tachycardia

9. Per-cutaneous coronary intervention in less than six months

10. Coronary Artery Bypass Graft kept before

11. Higher vulnerability / risk score.

The invasive strategy adopted is Coronary Arteriography followed by PCI or CABG according to the coronary anatomy. In long term, patient can be advised smoking cessation, daily exercise, weight reduction, blood pressure and glycemic control and lipid management along with anti-platelets, β-blockers, statins and ACE inhibitors.

ST SEGMENT ELEVATION MYOCARDIAL INFARCTION

Patho-physiology:

STEMI occurs following the occlusion of a coronary artery by a thrombus which causes reduced coronary blood flow abruptly in a previously atherosclerosed vessel. The plaque surface gets disrupted promoting thrombogenesis. Minor incidences shows, STEMI can occur due to other reasons like, coronary emboli causing occlusion of the affected vessel, vessel abnormities from birth genetically, spasm of the coronary arteries, and varied incidences of inflammatory disorders causing systemic effects.

In addition to common coronary risk factors, hyper coagulation state, collagen vascular disease, cocaine abuse, intra cardiac mass or thrombi producing coronary emboli are at increased risk of STEMI.

Clinical Features

Pain is a most common presenting complaint. There may be associated fatiguability, generalized body weakness, nauseating experiences, emesis, anxiousness and a feel of upcoming doom. Incidence of patients with STEMI without chest pain is greater if he is suffering from diabetes mellitus or immunosuppressant status in elderly. Most patients will be anxious and restless, show pallor associated with perspiration, cool extremities commonly. Patients with anterior infarction show evidence of sympathetic hyper activity like tachycardia, hypertension (in $1/4^{th}$ of the cases) and approximately 50% of patients with inferior infarction prove evidence suggestive of increased parasympathetic hyperactivity like decreased heart rate and blood pressure leading to collapse. Signs of ventricular dysfunction like S_3, S_4 and paradoxically split S_2 may be seen.

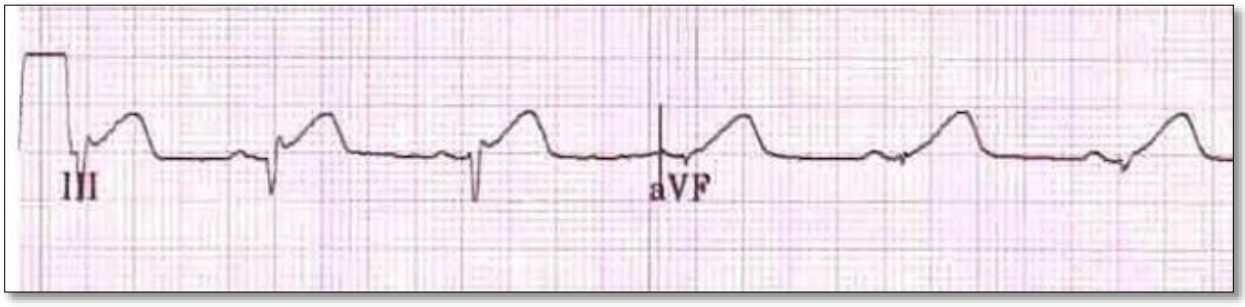
Investigations

The chief investigations are biomarkers, electrocardiogram & imaging.

1. ECG

The ECG manifestations of acute MI without LVH or LBBB are,

1. ST segment elevation≥0.2 mV in males or ≥ 0.15 mV in females in chest leads or > 0.1 mV in main leads.
2. Tall T waves



3. New ST depression of ≥ 0.05 mV either horizontally or sloping down in 2 continuous leads

   And/or T inversion ≥ 0.1 mV is 2 continuous leads with prominent R wave

   Or R/S ratio > 1.[9]

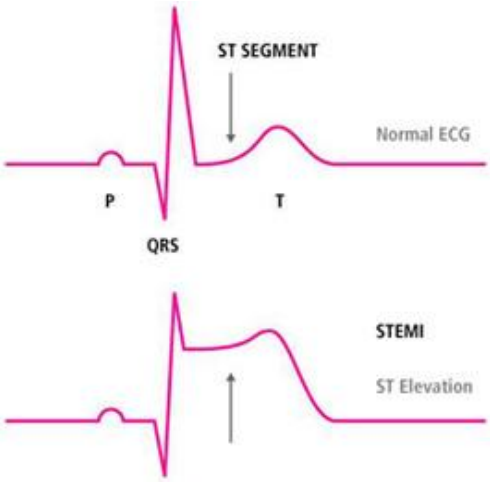


Figure 10 showing ECG in acute STEMI

1. Cardiac biomarkers

The preferred biomarkers are either Troponin I or Troponin T. It has high degree of absolute myocardial tissue specificity and sensitivity. It basically mirrors even the microscopic zones of Ischemic necrosis, usually expresses the measurement value more than 99 of a population used as reference. Blood samples are drawn on first assessment and 6-9 hours later. To establish the diagnosis, 1 elevated value above normal is required. If troponin is not available, CK-MB can be used.

2. Cardiac Imaging

Echocardiography is done to evaluate the thickness of the myocardium, motion of the myocardial walls at rest and its thickening. To detect areas of infarction, imaging studies like Cardiac Doppler, Contrast materials, Radio-nucleotide imaging and Cardiac MRI are used.[9]

Management

The first 24 hours is very crucial as majority of deaths occur within that period due to Ventricular Fibrillation. Therefore pre hospital care in the form of symptom recognition, early medical attention like cardiac resuscitation and reperfusion therapy is highly essential.

If hypoxemia is present O_2 should be administered at the rate of 2 to 4 litres per minute for first 6-12 hours.

Drug treatment includes

(1) ***Aspirin*** - for rapid inhibition of cyclo-oxygenase enzyme in platelets followed by reduction of thromboxane A_2 levels.

(2) ***Nitroglycerin (sublingual)*** - to control chest discomfort

(Exceptions –SBP $\leq$90 mm of Hg, Infarction of right ventricular wall)

(3) ***Morphine*** - Routinely administered for relief of pain which is often associated with STEMI by iv route in minimal doses (2-4 mg), at an interval of 5 min.

(4) ***β-blockers*** - they are used intravenously to avoid re-infarction risk and ventricular fibrillation. Oral beta blockers are initiated within first 24 hrs in patients who do not have Heart failure, CHB, Known Asthmatics, or any interstitial lung diseases.[11]

Next step in the management strategy is to decide between fibrinolysis and primary PCI. The primary aim is to confine the total span of ischemia within 120mins. If the patient cannot be transferred to a PCI capable hospital, fibrinolysis should be started within 30mins. If there is a contraindication for fibrinolysis or fibrinolysis became unsuccessful, an inter-hospital transfer should be considered, to a center where PCI is available, that too within 90 min.[12, 13]

High risk patients include those in cardiogenic shock, hemodynamic or electrical instability and persistent ischemic symptoms. They are the prime candidates for rescue PCI after failed thrombolysis.

Approach to the management of patients with ACS

UA/NSTEMI	All patients	STEMI
• Aspirin • Heparin (UFH or LMWH) • Clopidogrel In high risk patients: • Primary PCI • GP IIb/IIIa inhibitor	• Nitrates • Beta blocker • ± Ca channel blocker • Morphine • Oxygen Additional therapies shown to have long-term outcome benefits • ACE inhibitor • Statin	• Aspirin • Heparin (UFH or LMWH) • Clopidogrel Reperfusion method selected based on timing: • Primary PCI + GP IIb/IIIa inhibitor if performed within 90 mins of presentation • Fibrinolysis within 30 mins of presentation if timely PCI not possible

Table 4 – Approach to the management of Acute coronary syndrome

Complications

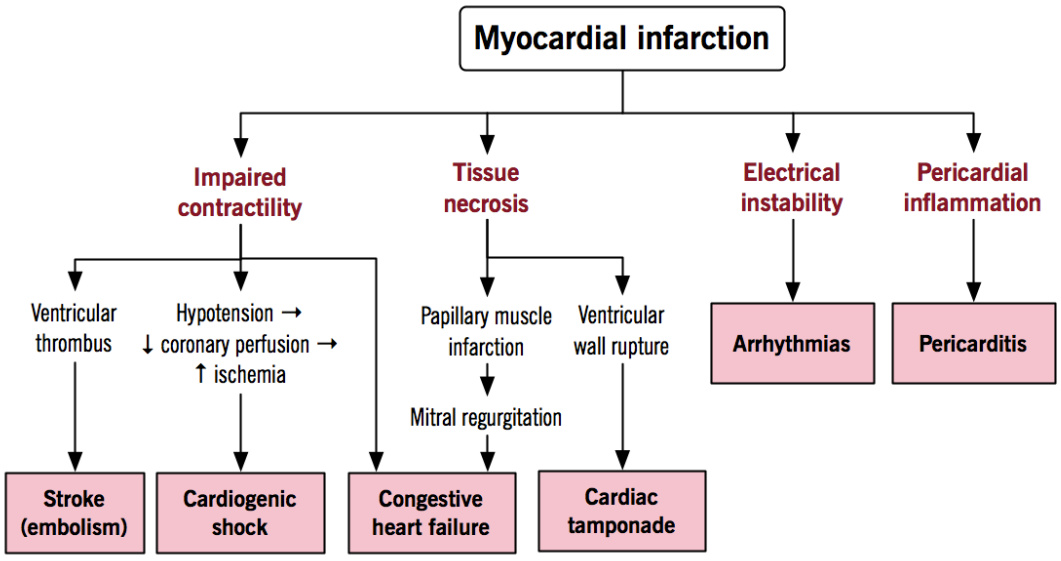


Figure 11 – Complications of myocardial infarction

Patient with STEMI can go in for

1. Ventricular dysfunction
2. Pulmonary edema
3. Cardiogenic shock
4. Right ventricular infarction
5. Arrhythmias
6. Recurrent chest discomfort/ re infarction
7. Pericarditis
8. Thromboembolism,
9. Left ventricular aneurysm.

Post infarction strategies

They include exercise stress testing before hospital discharge in stable patients, or 4-6 weeks after infarction in others. Coronary angiography, electrophysiological studies etc are advised accordingly. Secondary prevention is by anti-platelet drugs, ACE Inhibitors or ARB, or spironolactone in patients with Heart Failure, and warfarin in patients with high risk of embolism. Modification of risk factors promoting atherosclerosis is also essential for effective prevention of Myocardial Infarction.

PATHOLOGY OF MYOCARDIAL INFARCTION

MI is the ischemic necrosis of cardiac cells. It can be categorized into coagulation or contraction band necrosis. Cell death begins after a definite interval of time (as it can be minimal as about 20 minutes as per animal models) and it may take up to 2-4 hours to go in for complete necrosis or even longer. It can be classified as Acute, Healing or Healed based on the pathogenesis of events. Acute infarction can be easily identified by the presence of polymorphonuclear leucocytes. Whereas Healing MI is characterized by mononuclear cells and fibroblasts along with absence of PMNLs. In a Healed MI, there is scar tissue and absence of cellular infiltration, which usually takes about 5-6 weeks to form.[14]

Temporal classification of STEMI

EVOLVING	**< 6 hours**
ACUTE	6 hours – 7 days
HEALING	7 – 28 days
HEALED	>28 days

Table-5 : Temporal classification of STEMI

PROGNOSTIC MARKERS OF ACUTE MYOCARDIAL INFARCTION

1. ***Procalcitonin***

   A study made in the department of Cardiovascular Science, University of Leicester, about relationship between Plasma Procalcitonin and Acute Myocardial Infarction showed that, when the plasma level of procalcitonin increases beyond the median level, it shows adverse outcomes in subjects with Acute Myocardial Infarction. It is also associated with LV dysfunction and remodeling post MI.[16]

2. ***Heart rate variability, Arrhythmias and LV function***

   Kansas medical university hospital studies made between 2002 to 2004, concluded that LVESV, atrial fibrillation/ flutter and ionotropic agent administration on day 1 are independent predictors of prognosis in Acute MI[17]

3. ***Heart type Fatty Acid Binding Protein (H-FABP)***

   Another study involving 1448 subjects with coronary artery disease was done. H-FABP level was measured from a single blood sample which showed patient negative for both H-FABP and Troponin I has lower risk, compared to those with positive H- FABP and negative troponin. The latter had higher risk of death.[18]

4. ***Circulatory phospholipase A_2***

   Circulatory phospholipase A_2measured in patients with suspected acute coronary syndrome, help to distinguish between various causes of ST elevation in ECG. $SPLA_2$ is significantly higher in ACS than other varied causes of ST elevation.[19]

5. ***Cytokine - IFNr***

   Cytokine – IFNr stimulates the breakdown of tryptophan into kynurenine. elevated K-T ratio is an index of heightened incidence of worse prognostic events in stable coronary artery disease.[20]

6. ***Cell-free DNA levels***

   Cell free DNA levels that originate from cell death & circulating in peripheral blood were significantly higher in patients with Acute Myocardial infarction and play a role in prognosis.[21]

7. ***Serum Endoglin***

   It is a proliferation and hypoxia inducible protein expressed in endothelial cells. An observational prospective study came to the inference that post AMI mortality can be predicted based on an early change in serum endoglin.[22]

8. ***Cardiac Index and APACHE – II Scores***

   Cardiac index and both initial and serial APACHE - II scores provide reliable prognostic information, whereas the serial BNP values were not

predictive of mortality associated with complicated AMI, patient in cardiogenic shock.[23]

9. Circulating markers of collagen

Circulating markers of collagen - turn over are of prognostic utility following Acute Myocardial Infarction. Among plasma levels of N-terminal fragment of type1 collagen (PINP), carboxy terminal telopeptide of type 1 collagen (ICTP), matrix metalloproteinase (MMP-1) and tissue inhibitor of MMPS type 1 (TIMP-1). N terminal fragment of type 111 collagen (PIIINP). ICTP is indicative of better prognosis in MI, either in Acute or in Chronic.[24]

10. C- reactive protein

C- reactive protein in acute myocardial infarction monitoring is highly helpful in predicting the outcome along with uric acid and very low HDL levels. But it is not a specific index as it can rise in many other inflammatory conditions.[25]

11. Creatine kinase

Admission creatine kinase is a better prognostic predictor for a subsequent cardiac event, while Troponin T is a better predictor of mortality when we follow up for years. Together they do not improvepredictability.[26]

12. Growth differentiation factor-15

Gdf-15 - a member of TGF-β family, has a prognostic role in AMI patients, and is useful for predicting death and heart failure. It shows increased levels during periods of ischemia and reperfusion.[27]

13. N-terminal pro Brain Natriuretic peptide

It can be used for risk stratification of NSTEMI and unstable angina. Among patients classified as low risk by an LVEF> 55%, negative Troponin T and a TIMI risk score of ≤4, NT pro BNP levels>331 ng/L predicted adverse clinical outcome.[28]

14. Troponin T

Troponin I and T are sensitive indicators of Acute Myocardial Infarction. But they can't be considered as specific, as there are many conditions where the Troponin levels are falsely elevated.

False elevation of Troponin

1. Cardiac contusion
2. Congestive heart failure
3. Aortic dissection

4. Aortic valve disease
5. Hypertrophic Cardiomyopathy
6. Arrhythmias
7. Apical ballooning syndrome
8. Rhabdomyolysis with cardiac injury
9. Pulmonary embolism
10. Kidney Failure
11. Cerebro-vascular Accidents or SAH
12. Drug toxicity
13. Storage Disorders - Amyloidosis, Sarcoidosis
14. Scleroderma, Haemochromatosis
14. Inflammatory Myocarditis
15. Drug toxicity
16. Sepsis
17. Burns
18. Extreme exertion[15]

SCORING SYSTEMS FOR MI

- TIMI Score
- GRACE Score

- PURSUIT Score
- GESSI Score

1. TIMI Risk Scoring (Thrombolysis in Myocardial Infarction Score)

In 1984, Eugene Braunwald made a study group in association with Brigham and Women's Hospital and Harvard Medical School. This group was later called as TIMI group. It is used to predict the risk of death and also the ischemia associated problems in Unstable Angina or an NSTEMI.[29]

TIMI RISK SCORE for UA / NSTEMI

HISTORICAL	POINTS
Age ≥ 65	1
≥ 3 CAD risk factors (FHx, HTN, ↑ chol, DM, active smoker)	1
Known CAD (stenosis ≥ 50%)	1
ASA use in past 7 days	1
PRESENTATION	
Recent (≤ 24H) severe angina	1
↑ cardiac markers	1
ST deviation ≥ 0.5mm	1
RISK SCORE=Total Points (0-7)	

RISK OF CARDIAC EVENTS (%) BY 14 DAYS IN TIMI 11B*

Risk Score	Death or MI	Death, MI or Urgent Revasc
0/1	3	5
2	3	8
3	5	13
4	7	20
5	12	26
6/7	19	41

*Entry criteria: UA or NSTEMI defined as ischemic pain at rest within past 24H, with evidence of CAD (ST segment deviation or +marker)

Table 6 – TIMI risk score for NSTEMI

Mortality Risk Calculation Using TIMI Score

TIMI Score shows a mortality rate of more than 35% when the score crosses 8/14. Hence the mortality associated with STEMI is higher compared to NSTEMI.[30]

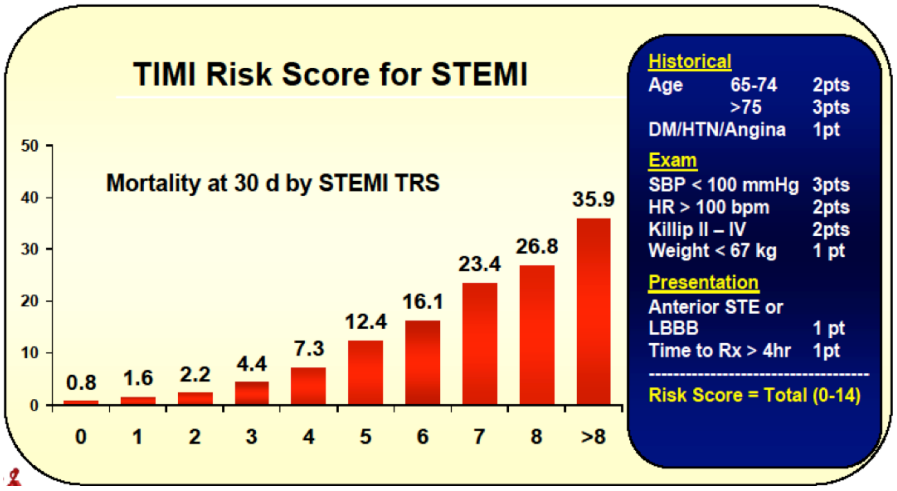
TIMI RISK SCORE for STEMI

HISTORICAL	POINTS
Age ≥ 75	3
65-74	2
DM or HTN or angina	1
EXAM	
SBP < 100 mmHg	3
HR >100 bpm	2
Killip II-IV	2
Weight < 67 kg (150 lb)	1
PRESENTATION	
Anterior STE or LBBB	1
Time to Rx > 4 hrs	1
RISK SCORE = Total points (0-14)	

RISK SCORE	30-DAY MORTALITY IN InTIME II(%)*
0	0.8
1	1.6
2	2.2
3	4.4
4	7.3
5	12
6	16
7	23
8	27
>8	36

*Entry criteria: CP > 30 min, ST ↑, sx onset < 6hrs, fibrinolytic-eligible

Table 7 – TIMI risk score for STEMI



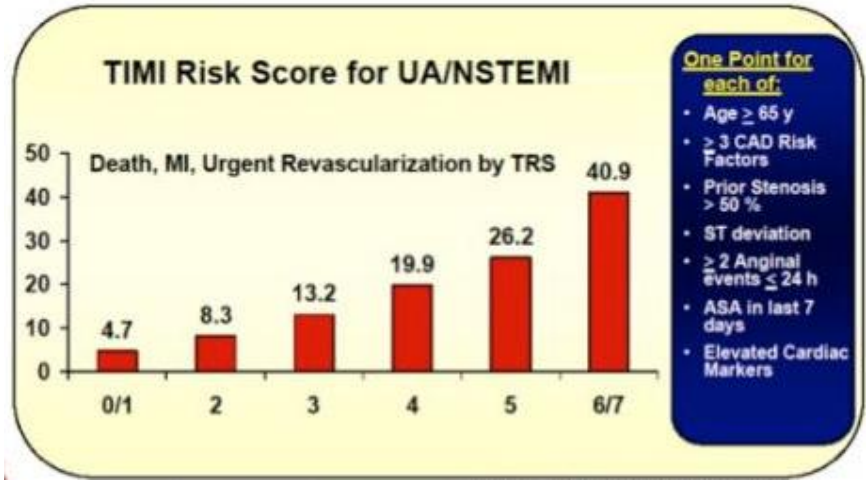


Figure 12 – TIMI scores and mortality risk in STEMI and NSTEMI

2. GRACE Score

Background		Findings at time of admission		Findings during hospital stay	
① Age, y	Points	④ HR at admission, bpm	Points	⑦ Serum creatinine at admission, mg/dL	Points
≤ 29	0	≤ 49.9	0	0-0.39	1
30-39	0	50-69.9	3	0.4-0.79	3
40-49	18	70-89.9	9	0.8-1.19	5
50-59	36	90-109.9	14	1.2-1.59	7
60-69	55	110-149.9	23	1.6-1.99	9
70-79	73	150-199.9	35	2-3.99	15
80-89	91	≥ 200	43	≥ 4	20
≥ 90	100	⑤ SAP at admission, mmHg		⑧ Elevated enzymes or markers	15
② History of heart failure	24	≤ 79.9	24	⑨ No percutaneous revascularisation	14
③ History of AMI	12	80-99.9	22		
		100-119.9	18		
		120-139.9	14		
		140-159.9	10		
		160-199.9	4		
		≥ 200	0		
		⑥ Depressed ST segment	11		

Table 8 – components of GRACE score

Sensitivity of both GRACE and TIMI are similar. ($p = 0.79$, not significant; while Specificity of GRACE score is significantly higher than that of TIMI Score ($p < 0.001$)

Comparison between TIMI and GRACE Score

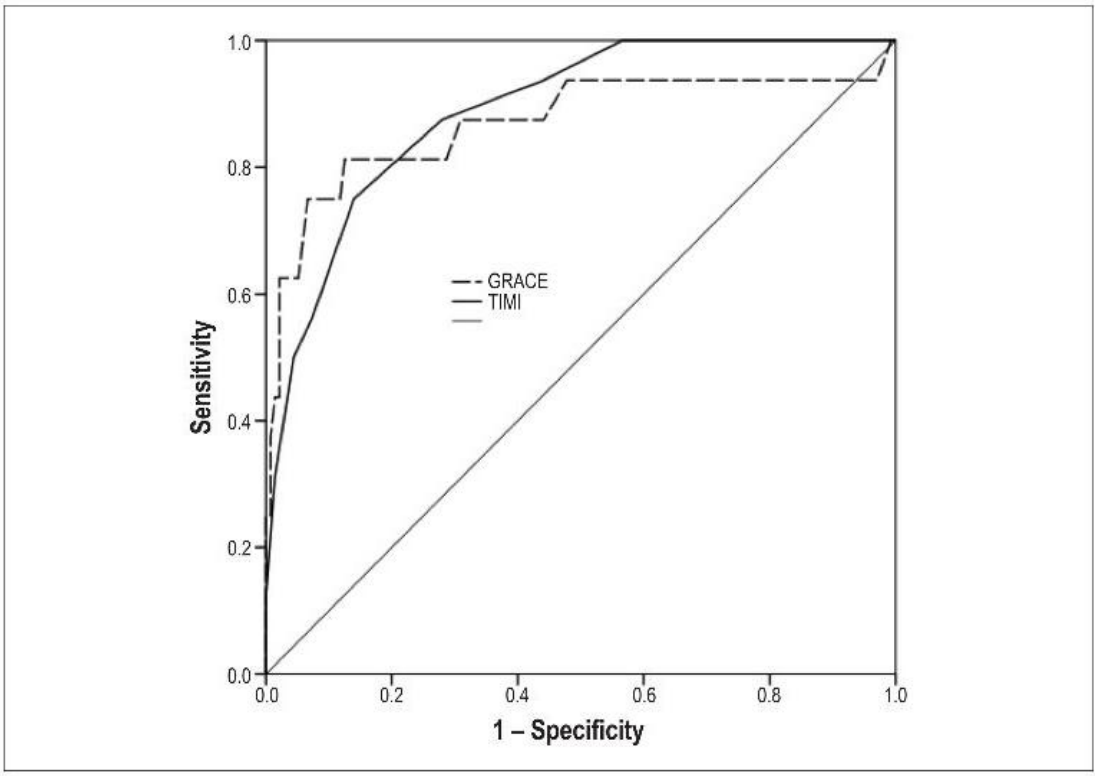


Figure – 13 TIMI vs GRACE

3. PURSUIT Score

Risk Score is calculated with Age (0–14 points), Sex (1 if male), Chest pain (0–2), Heart Rate (0–5), SBP (0–2), ST-segment depression (1–3), and signs of heart failure (2–3). It was developed after a multinational RCT (Platelet Gp2b3a in Unstable angina: Receptor Suppression Using Integrilin Therapy). Patients are classed for risk for death at 30 days into low, intermediate and high risk.

KILLIP'S CLASSIFICATION

Killip and Kimball described 250 patients treated with AMI in a specialized ICU, who were managed based on risk stratification - reported improved mortality &morbidity in those patients (1967).[31]

Killip Subgroup	Clinical characteristics	Hospital mortality
I	No congestion signs	<6%
II	S3, basal rales	<17%
III	Acute pulmonary edema	38%
IV	Cardiogenic shock	81%

Killip classification.

- Stage I— No heart failure. No clinical signs of cardiac decompensation;
- Stage II— Heart failure. Diagnostic criteria include rales, S3 gallop and pulmonary venous hypertension. Pulmonary congestion with wet rales in the lower half of the lung fields;
- Stage III— Severe heart failure. Frank pulmonary oedema with rales throughout the lung fields;
- Stage IV— Cardiogenic shock. Signs include hypotension (SBP 90mmHg), and evidence of peripheral vasoconstriction such as oliguria, cyanosis and diaphoresis.

URIC ACID

When Cell death occurs, purine from the nucleic acids gets released and metabolized to form Uric acid, chemically, $C_5H_4N_4O_3$. Uric acid occurs widely in nature in the form of its salts, found in plants as well as in animals. It is a heterocyclic compound.

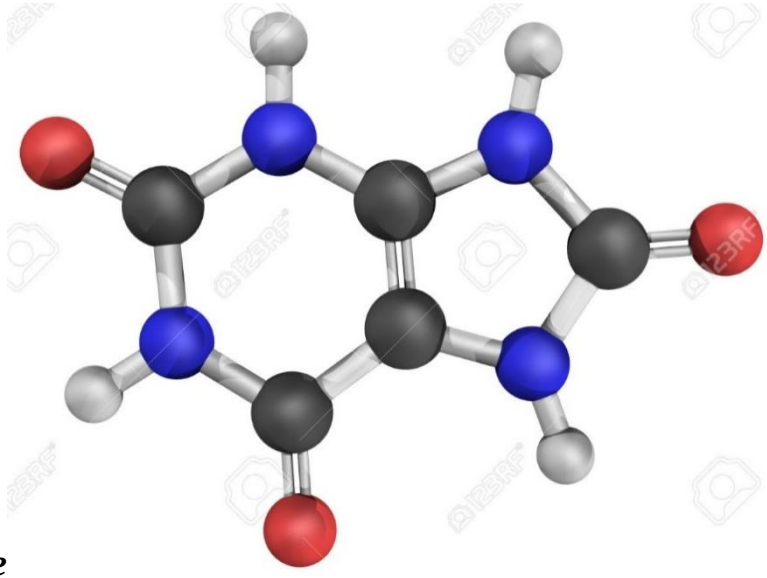
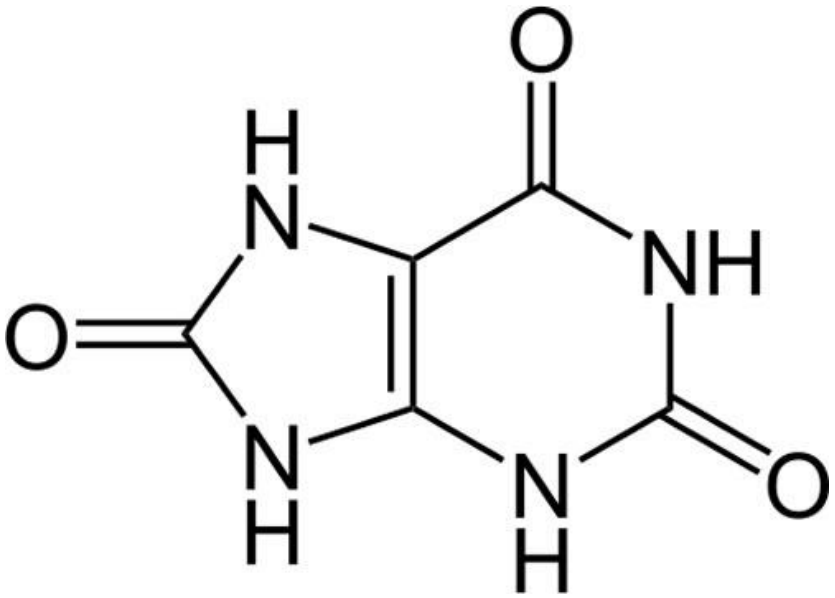


Fig14 : Uric Acid Structure



Uric acid circulates as urate ion at normal arterial pH. Uric acid is not converted to allantoin so urates are regularly excreted in urine. The enzyme xanthine oxidase makes uric acid from xanthine and hypoxanthine, produced from Purines[32.]Uric acid production in human beings, uric acid is produced in the liver, along with dietary contribution.

GMP, IMP, AMP →ultimately into guanine hypoxanthine→ xanthines

Xanthine irreversibly oxidized to produce uric acid

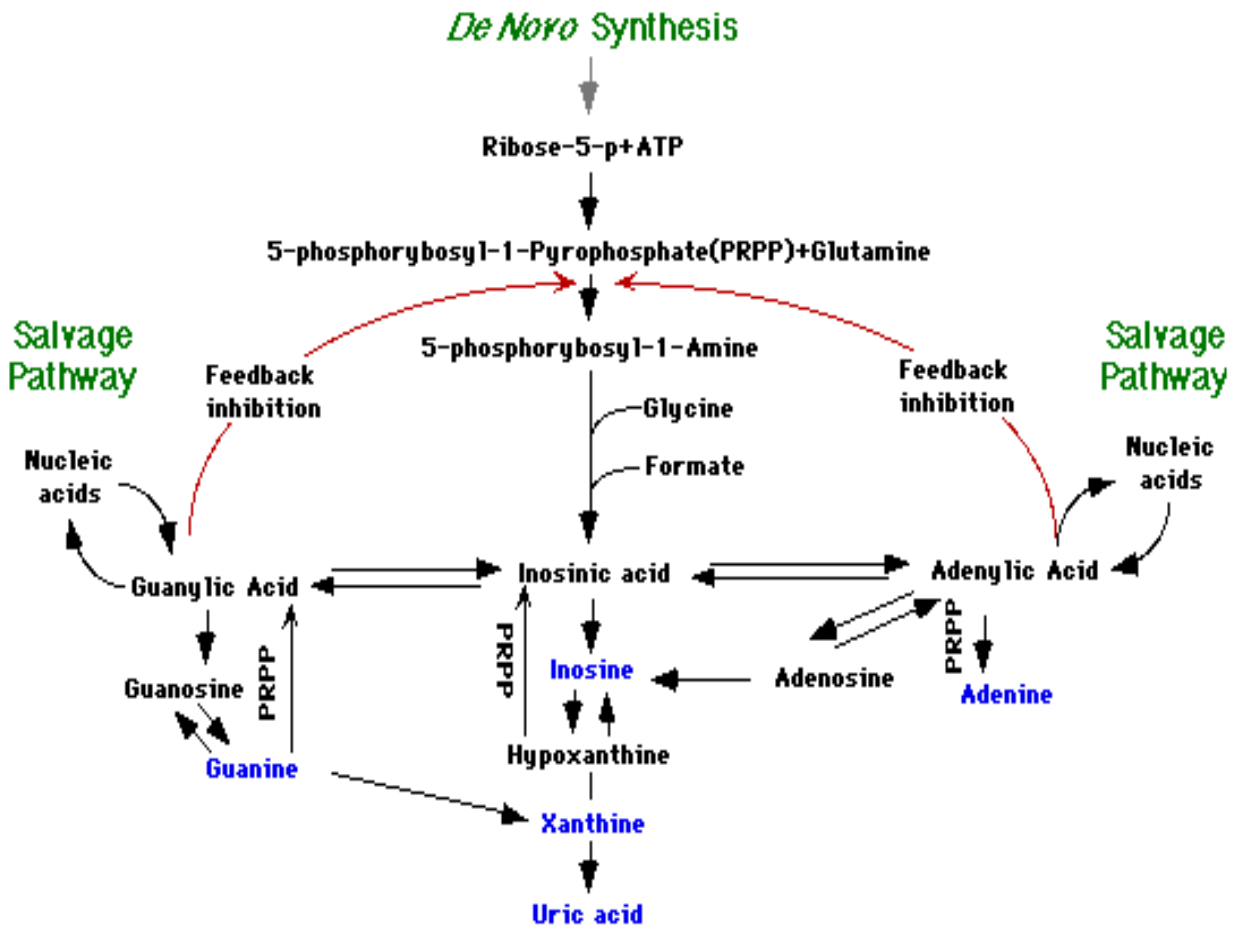


Figure 15 Uric acid pathway

Dietary sources

Purine is highly present in different organic meals such as cod liveroil, breads, fishes, green leafy vegetables, and mushroom, fish like mackerel, herrings, sardines and mussels, yeast, bacon, beef, oatmeal, kidney beans, lentils etc are other sources of uric acid that is commonly available.[33]

Excretion of uric acid

Minor contribution in digestion of uric acid is by peroxidases and catalases. Elimination of uric acid in mainly through the GIT and kidneys. 1/3rd of total uric acid in digested by intestinal uricolysis.[34] Two thirds is via the kidney. The transporters were URAT1 transporter (found only in proximal renal tubule inhibited by lactate and ketone bodies)[35.] $GLUT_9$ -reabsorbs urate into

circulation. $GLUT_9$ was previously identified as fructose transporter. Probenacid& benzo-bromarone inhibits these transporters.[33]

Normal uric acid levels vary in sex and also show day to day and seasonal variations.

Adult men : 2 to 7.5 mg/dl

Adult women : 2 to 6.5 mg/dl.

In Early months of pregnancy, uric acid declined by 1/3rd; but by term the level rises to non-pregnant level.

Men $\geq$ 40 yrs: 2 to 8.5 mg/dl

Women $\geq$ 40 yrs: 2 to 8.0 mg/dl &

There will be a rise in relation to menopause.

The normal level of uric acid in urine will be 250-750 mg over 1 day period. Reference values need to be checked before each time we go in for Uric acid testing.

Increased levels of uric acid/ Hyperuricemia Seen with,

Due to urate super saturation / 2^0 to decreased excretion, over production.

CAUSES OF HYPERURICEMIA	
Gout	Hemolytic anaemia
Renal failure	Chemotherapy
Alcoholism	Radiation
Dehydration	Enzyme deficiencies
Leukemia and lymphoma	Psoriasis
Starvation	Obesity
Metabolic acidosis	Glycogen storage disease
Toxemia of pregnancy	Chronic renal disease
Infectious mononucleosis	Lead nephropathy
Hyperlipidemia	

Table 10 – causes of Hyperuricemia

Decreased levels of serum uric acid/ Hypouricemia seen with,

Occurs due to decreased production or increased excretion.

1. Transporter defect - familial renal hypouricemia
2. Fanconi syndrome
3. SIADH - volume expansion
4. Hodgkin's lymphoma
5. Cerebral salt wasting - intracranial disease

6. Vitamin C can reduce blood uric acid level[37]
7. Cherry juice - has shown to reduce uric acid when given to marathon runners.
8. Xanthine oxidase deficiency, purine nucleoside phosphorylase deficiency

Uric acid and genetics

The serum uric acid level in siblings of gouty patient was higher than siblings of controls. These observations were confirmed by the study of black foot and Pima Indians. The frequency distribution of uric acid is Gaussian/normal in general population.[38]

In the study of 6000 subjects from Tecumseh community health study showed multi factorial inheritance with additive gene action interacting with environmental factors to produce serum uric acid phenotype.[39]

URIC ACID AND DRUGS

Drugs that causes Hyperuricemia:

Alcohol

Ascorbic acid,

Aspirin

Caffeine

Cisplatin

Diazoxide

Diuretics

Epinephrine

Ethambutol

Levodopa

Methyldopa

Nicotinic acid

Phenothiazines

Theophylline

Drugs that causes Hypouricemia:

1. Allopurinol
2. Azathioprine
3. Clofibrate
4. Corticosteroids
5. Estrogen
6. Glucose
7. Guaifenacin
8. Mannitol
9. Probencid
10. Warfarin

Uric acid and oxidative stress

When Uric Acid is synthesized, there is production of ROS leading to increased vascular oxidative stress.[40] Xanthine oxido reductase, is a hepatic enzyme, which catalyse uric acid, produce ROS and damage the nucleic acids. XOR can be interchanged into two different forms XO- Xanthine oxidase, XDH -Xanthine dehydrogenase. XO cannot reduce NAD^+, unlike XDH, XO prefers molecular oxygen.[41]

Allopurinol, a xanthine oxidase inhibitor, decrease uric acid levels and is beneficial by

1) Decreasing ROS,

2) Myocardial contraction is enhanced due to restoration of sensitization to calcium and its response to β adrenergic receptors,

3) Preventing xanthine oxidase mediated intermittent hypoxia induced vasculardysfunction.[42]

Uric acid as antioxidant

Uric acid is an effective scavenger of all the free radicles produced, and also a chelator of ions of may minerals especially transitional metals. Which in turn

gets converted to inactive or less active forms.[43]These ideas are supported by both invitro and invivo studies[44].

Urate act as antioxidant by

1. Reducing Lipid Peroxidation & Preventing RBC Aging,
2. A Scavenger of Singlet Oxygen and Hydroxyl Radicals.[46]
3. Scavenger of Oxo-Heme Oxidants. Plasma Urate Levels Are Higher than ascorbate making it a major antioxidant .[47]

Uric acid and metabolic syndrome

Metabolic syndrome is a group of diseases or disease risk factors, a like insulin resistance, hypertension, glucose intolerance, elevated triglycerides and HDL levels is a major public health problem.[48]

Recent evidence suggest that uric acid may have a role in metabolic syndrome pathogenesis[49]and decreasing uric acid levels can reverse the features of MetS. Hyperuricemia is associated with android type obesity, not the gynoid type. Study done among the sumo wrestlers and Tecumsech community health study showed definite association between elevated serum uric acid and obesity.[50]

Molecular explanation for association between hyperuremia and MetS is high dietary carbohydrate intake (especially fructose or sucrose). In initial stages of obesity, elevated plasma fatty acids are responsible for the increase in uric acid levels. Fructose enters hepatocytes, metabolized by fructokinase, generates uric acid at the same time increase biosynthesis of TG, VLDL excretion and LDL over production.[51]

Uric acid and hypertension

Progetto hypertension Umbria MonitoraggioAmbulatoriale (PIUMA) study - PIUMA database was analysed to assess the association of serum uric acid and hypertension. Uric acid is bound for 5% of plasma proteins, freely filtered at the glomerulus, 99% reabsorbed in the proximal tubule and majority are reabsorbed. Thus a direct association exists between serum uric acid and renal vascular resistance, probably linking systemic hypertension and hyperuricemia.[52] Animal models suggest endothelial dysfunction, reduction in nitric oxide levels, activation of RAAS and vascular smooth muscle proliferation as causes of hypertension in hyperuricemia. The more impaired the kidney function, the more the level of serum uric acid along with impaired blood pressure control.[53] Moreover factors responsible for oxidative stress, polymorphic changes of transporters achieved genetically and functionally also needs consideration.

Uric acid and diabetes mellitus

Lower serum uric acid was found in diabetics, higher levels in pre-diabetics compared to non-diabetic subjects.[54] Hyperuricemia is a function of decreased renal function. The positive association between hyperglycemia of 8mmol/l (upto 8mmol/l) is not dependent on BMI, alcohol intake, gout or diuretic treatment of hypertension and it probably reflects the interaction between glucose and purine metabolism, via the phosphorylation of glucose to glucose-6-phosphate.[55] Diabetes and non diabetics with a blood sugar level more than 8 mmol/l showed lower uric acid level, thus an effect of hyperglycemia rather than the use of oral anti-diabetic drugs.

Hyperuricemia is presumed to be a consequence of insulin resistance rather than its precursor. When considered as a risk factor for diabetes mellitus, will be helpful if we can add uric acid lowering drugs in asymptomatic hyperuricemia, reducing the chance of type 2 diabetes mellitus.[56]

Serum uric acid and Cancer

Uric acid is potentially more important as an antioxidant in normal physiology. A positive association was detected between antecedent serum uric acid and subsequent development of prostate cancer within an interval of 10-15 years but not with any other cancer site.[57]Hialt and Fireman found no relation of

uric acid in the blood with cancer prevalence after adjustment for age, race, education, tobacco consumption, alcoholism, and BMI.[58]

Serum uric acid in smokers

Cigarette smoke a source of oxidative stress on chronic exposure lead to low uric acid levels in smokers, when arranged excluding other risk factors. As the reduction in uric acid levels is proportional to smoking status and predispose to cardiovascular disease, the study recommends to quit smoking & introduce uric acid estimation as a routine test.[59]

Serum uric acid and neurological disease

Hypouricemia produces reduced free radical scavenging capacity of the body like peroxynitrate which in turn can produce cell damage. This is how uric acid acts as a neuro-protectant. Moreover astroglia must be present for uric acid to act. Uric acid acts on astroglia and up-regulate EAAT-1, a glutamate transporter thereby protect spinal cord. Thus an astroglia mediated mechanism is behind the neuroprotection by uric acid.[60]

SUA and Gout

Monosodium urate crystal deposition leads to a painful rheumatic disease called gout. When concentration of uric acid is above 380 µ mol/L or 6.8 mg/dl it will precipitate. Disease is more common in men, as hyperuricemia can produce

gout, even low levels of serum uric acid can cause gout . gout can be due to purine rich diet, diuretic therapy, alcoholism and metabolic syndrome. Gout can be classified as primary (if no identifiable cause is present) or secondary. Treatment of gout includes lifestyle modification, nutrition, uric acid lowering drugs, like - xanthine oxidase inhibitors, uricosurics, uricase agents.[61]

The different stages of gout includes

I - Asymptomatic hyperuricemia,

II - Acute flares,

III - Intercritical segments

IV - Advanced gout.

SUA and Heart Failure

Serum uric acid levels are elevated in patients with congestive heart failure, because of 1) parallel worsening renal function, 2) over protection of uric acid, 3) restricted sodium intake and use of diuretics. Thus the use of diuretics in patient with heart failure, will increase SUA, and thereby plasma UA mediated antioxidant capacity, making diuretics beneficial in CHF prognosis.[62]

SUA and Renal diseases

Very high levels of uric acid can produce renal insufficiency which rapidly progressive. More prolonged form of hyperuricemia leads to a chronic tubule interstitial disorder - gouty nephropathy. Hyperuricemia can lead to nephrolithiasis too.[63]

Regarding Hyperuricemia & renal diseases the features include

1) Intrarenal crystal deposition,

2) vasoactive & pro inflammatory effects[64],

3) Renal disease progression,

4) male gender affected more[65],

5) hypertension, proteinuria[65], renal dysfunction, vascular disease and progressive renal scaring,

6) activation of RAAS and COX - 2 system.

Uric acid nephropathy - can be oliguric or anuric, due to over production or under excretion of uric acid with serum levels >15 mg/dl. The Uric Acid to S. Creatinine ratio is >1 (0.6-0.7 in other AKIS). Associated features are hyperkalemia, hypocalcemia and hyperphosphatemia. Acute nephropathy is treated with I/V hydration, allopurinol or rasburicase.

If chronic nephropathy-uric acid crystal deposits in the medullary interstitium, results in chronic inflammation, interstitial fibrosis and chronic kidney diseases. If UA>9 with creatinine <1.5, UA > 10 with serum creatinine 5- 20, UA > 12 with advanced renal failure chronic nephropathy can be suspected in CKD patients.

Familial juvenile hyperuricemic nephropathy (MCKD type 2)

It is an autosomal dominant inherited disease with gout and progressive renal impairment.

LITERATURE SUPPORTING THE STUDY

In low risk group population of CVD; SUA is a relatively reliable predictor, but it gains high significance in high risk groups.[66] Independent association of uric acid with severity of atherosclerotic plaque in coronary vessels, has been attained in a cross sectional study of Turkish patients. Korean studies using angiography supported this association of SUA with non-modifiable risk factors of atherosclerosis.[61]

Uric acid and acute MI

1. In a retrospective study done in a hospital in Croatia, higher in-hospital mortality as well as thirty days mortality was observed in patients with higher serum uric acid levels, the study population being patients with acute

myocardial infarction, who presented within 48 hours of onset of symptoms. The long term survival was also worse in this group. Confounding factors were not found between SUA levels and myocardial infarction. Elevated creatinine value has also been found to be a good predictor of deaths following acute MI [67].

2. Cross sectional study among Chinese males revealed that hyperuricemia causes elevated blood pressure and stiffness of arterial vessels[68]. Contrary to this, a study done in Korea suggests that there is no correlation between SUA levels and arterial wall pliability. The index that was used to assess the association between hyperuricemia and arterial stiffness was brachial-ankle pulse wave velocity. The proposed mechanism for the same in hyperuricemia, is the production of superoxide radicals and oxidative stress, causing the development and progression of stiffness of vessels.[69]

3. A descriptive analytic research with non-random sampling in Zanjan Behesti Hospital in 2001, to assess the relationship between serum uric acid levels and AMI- concluded that:

   (1) uric acid levels increase with age, no change with sex.

   (2)a positive correlation exists between hyperuricemia and hypertension.

   (3) no meaningful relationship between smoking or diabetes mellitus with serum uric acid.[70]

4. In Beijing, China 502 patients with STEMI were studied to assess uric acid levels. Moreover serum lipid level and echocardiography data in hospital MACE were compared between hyperuricemia and non hyperuricemia. It was concluded that there is a positive correlation between SUA and triglyceride level, but it was not related to the severity of CAD.STEMI patients with elevated SUA have higher incidence of systolic and diastolic dysfunction and more major adverse cardiovascular events (MACE) while in hospital.[71]

5. Rotterdam study, which was a large prospective population based study, included 4385 participants who, at the beginning of the study, were more than 55 years and free from CAD and stroke. They were followed up until January 2002 and the study revealed that SUA is a strong risk factor for MI and stroke.[72]

6. In India, a study done in Seth GS hospital and KEM Mumbai assessed the close correlation between SUA levels and Killips classification in acute MI in 100 patients, by measuring serum uric acid level on days 0,3 and 7. The conclusion were:

(1) high SUA concentration in patients with MI on admission day and in patients with history of MI in the past.

(2) high SUA in patients with higher Killip class on all 3 days

(3) Killip class and uric acid combined together,is a good predictor of mortality in acute MI.[73]

7. Using Japanese acute coronary syndrome database, assessment of 1124 patients, who were hospitalised within 48 hours of MI, was done. Conclusions were as follows:

(1) there is a close relation between SUA and Killips class.

(2) SUA levels, killips class, peak CPK levels and age had significant predictive value of long term mortality.

(3) SUA level is a good indicator for predicting adverse cardiac events in the future. Together with Killips class , it forms a good mortality predictor.[74]

8. Framingham heart study was done to assess the relation of uric acid to incident CAD and death and it concluded that :

(1) there is no causal role for uric acid in the development of CAD or death due to cardiovascular disease .

(2) any apparent association could be attributed to the association of SUA with other risk factors

METHODOLOGY

MATERIALS AND METHODS:

Study design- prospective non interventional observational study

Study setting- medical ICU, CCU and internal medicine wards of GMKMCH Salem.

Duration of study – 100 consecutive cases of 2015- 2017.

INCLUSION CRITERIA:

- Age>18 years
- ST Elevation Myocardial infarction
- Non ST Elevation Myocardial infarction

EXCLUSION CRITERIA:

- Chronic kidney disease
- Patients with prior myocardial infarction
- Gout
- Hematological malignancy
- Patients on drugs like salicylate, ethambutol, pyrazinamide

SAMPLE SIZE:

100, out of which 55 STEMI and 45 NSTEMI were included.

PROCEDURE IN DETAIL:

The study was conducted in 100 cases of acute myocardial infarction patients admitted to our hospital. Patients are selected according to inclusion and exclusion criteria from internal medicine and cardiology departments of Government Mohan Kumaramangalam Medical College Hospital. Diagnosis of myocardial infarction is based on chest pain>20 minutes, ECG changes and elevation of cardiac biomarkers(two out of three). Detailed history and physical examination with special reference to Killip classification were carried out. Patients were followed up for a period of 7 days or discharge ,whichever is earlier. Uric acid values were measured on days 0 and 3, and other necessary values for exclusion were collected on first day of admission, and mortality/morbidity rates calculated in the first week of admission. A venous blood sample was collected to measure uric acid by venepuncture, preferably fasting for the last 4 hours, unless told otherwise. Uric acid was measured using autoanalyser, using the modified Trinder technique in our clinical biochemistry laboratory ,with value>8mg/dl considered as hyperuricemia. Diabetes was diagnosed according to ADA criteria or if patient is on treatment with oral hypoglycemic agents or insulin. Hypertension was diagnosed by SBP>140 and DBP> 90, average of two readings taken. Smoking at least one cigarette per day, for

everyday during the year was considered as current smoker. Cardiac biomarker used for study was Troponin T.

STATISICAL ANALYSIS

The study design was a prospective non interventional observational study. All data collected were noted using a structured proforma, including the investigations. Data was analysed using statistical package and SPSS structured software to find out the significance of serum uric acid as prognostic marker in myocardial infarction.

FUNDING AGENCY: none.

ETHICAL CONCERNS: as per the institution protocol.

CONSENT: informed consent was taken as per standard procedure that is followed in the institution.

RESULTS and OBSERVATIONS

This was a prospective, observational and non interventional study. The study population had 100 subjects.

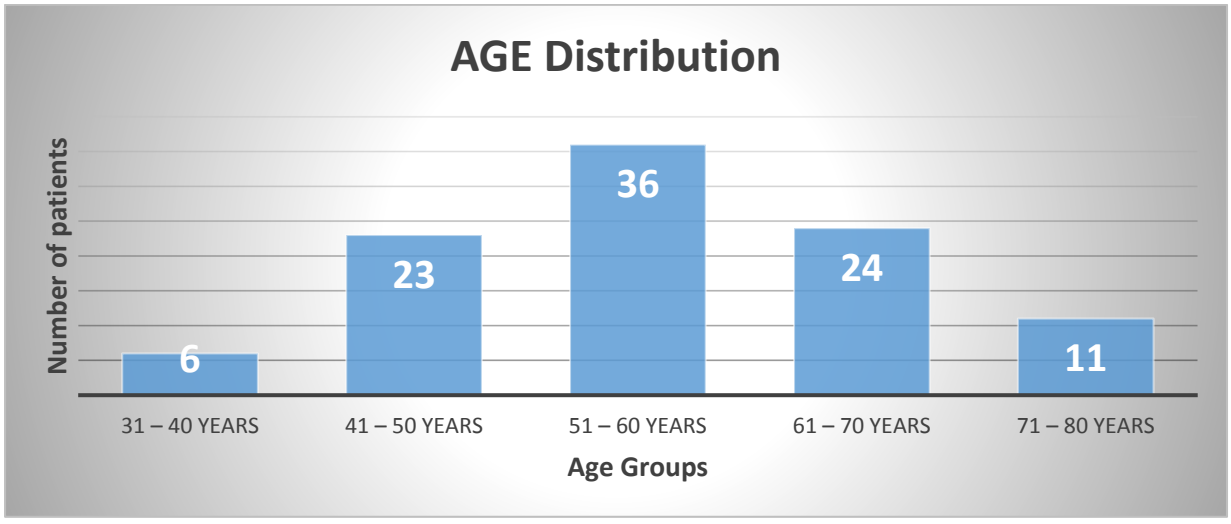
1. AGE DISTRIBUTION

The average age of the study group was 57.16 years. 36% of the patients belonged to the age group between 51 to 60 years. The age of the subjects ranged from as low as 34 years to as high as 80 years.

TABLE – 11 SHOWING AGE DISTRIBUTION IN THE STUDY POPULATION

AGE	Number of Patients (n)	Percentage (n%)
31 – 40 years	6	6 %
41 – 50 years	23	23 %
51 – 60 years	36	36 %
61 – 70 years	24	24 %
71 – 80 years	11	11 %

CHART – 1 BAR GRAPH showing AGE DISTRIBUTION OF THE STUDY POPULATION



2. GENDER DISTRIBUTION

Among the 100 subjects, there were 66 males and 34 females

TABLE 12 – GENDER DISTRIBUTION OF THE STUDY POPULATION

SEX	Number of patients (n)	Percentage (n%)
Male	66	66%
Female	34	34%

CHART 2 – GENDER DISTRIBUTION OF THE STUDY POPULATION

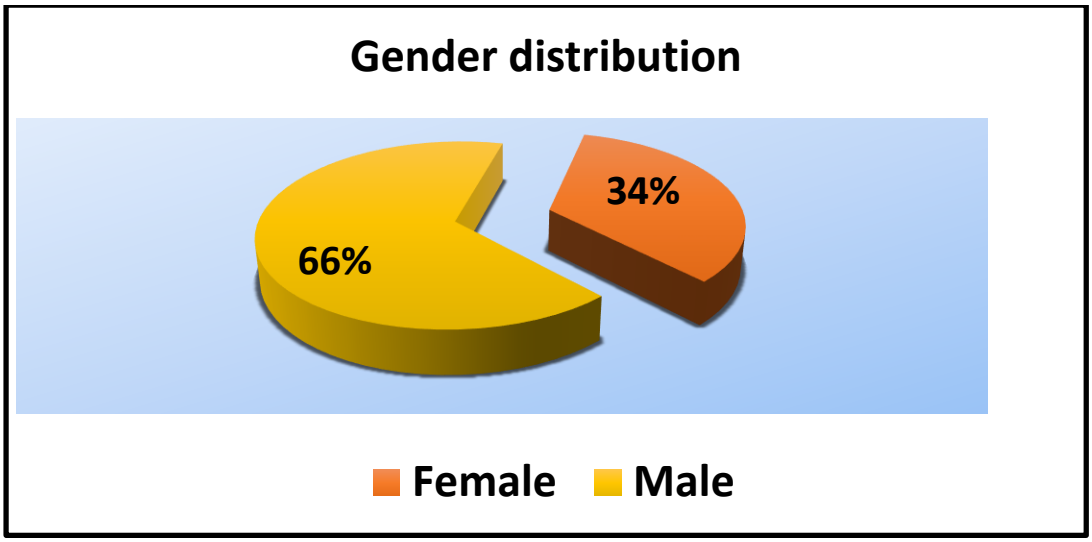
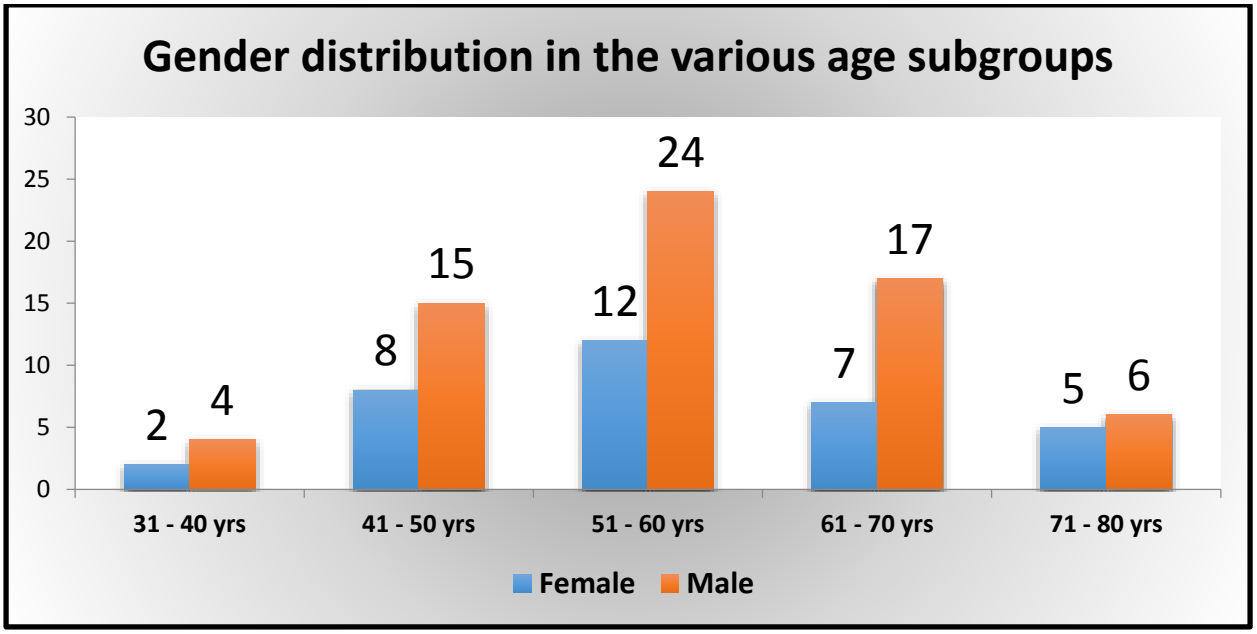


TABLE 13 – AGE and GENDER distribution

AGE	Males	Females
31 – 40 years	4	2
41 – 50 years	15	8
51 – 60 years	24	12
61 – 70 years	17	7
71 – 80 years	6	5

CHART 3 – BAR GRAPH showing AGE and GENDER CORELATION IN THE STUDY POPULATION

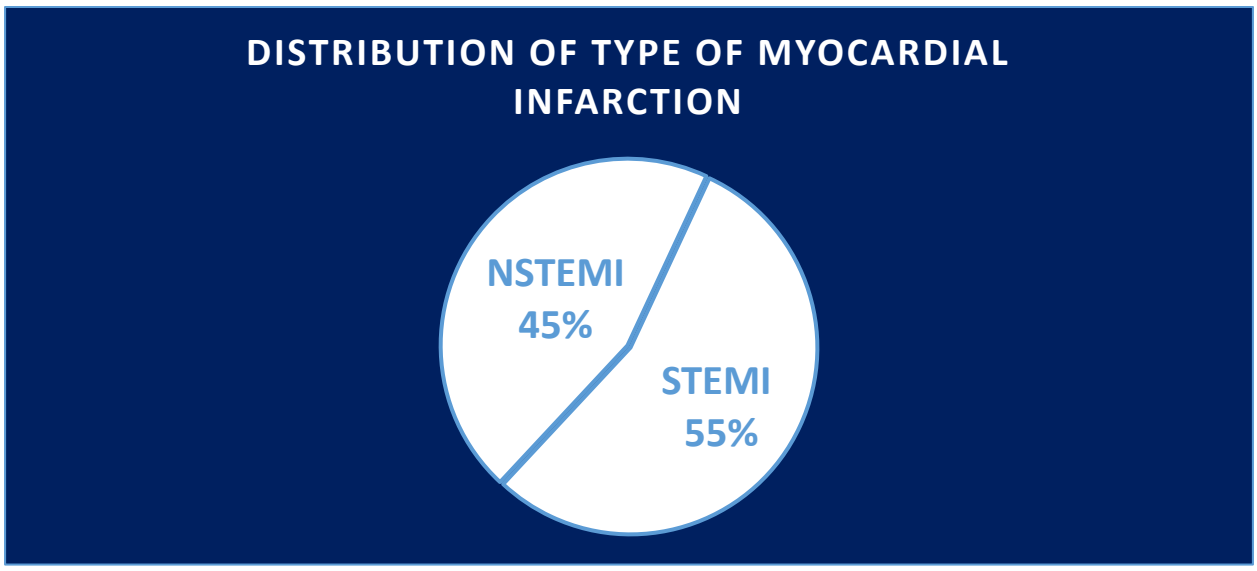


There is a predominance of males in all the age subgroups in the study.

3. TYPE OF MYOCARDIAL INFARCTION

There were 45 cases of NSTEMI and 55 cases of STEMI in the study population.

CHART 4 : PIE CHART showing TYPE OF MYOCARDIAL INFARCTION



4. MORTALITY STATISTICS

9 deaths occurred in the study group of 100 patients. 8 patients had died of ST elevation MI and 1 patient died of Non ST elevation MI. Out of the 9 deaths that occurred, 6 were males and 3 were females. χ^2 value was 0.965 and this was not found to be statistically significant. Most of deaths occurred in the age group 50 to 70 years (77.78%)

CHART 5 : MORTALITY IN THE STUDY GROUP

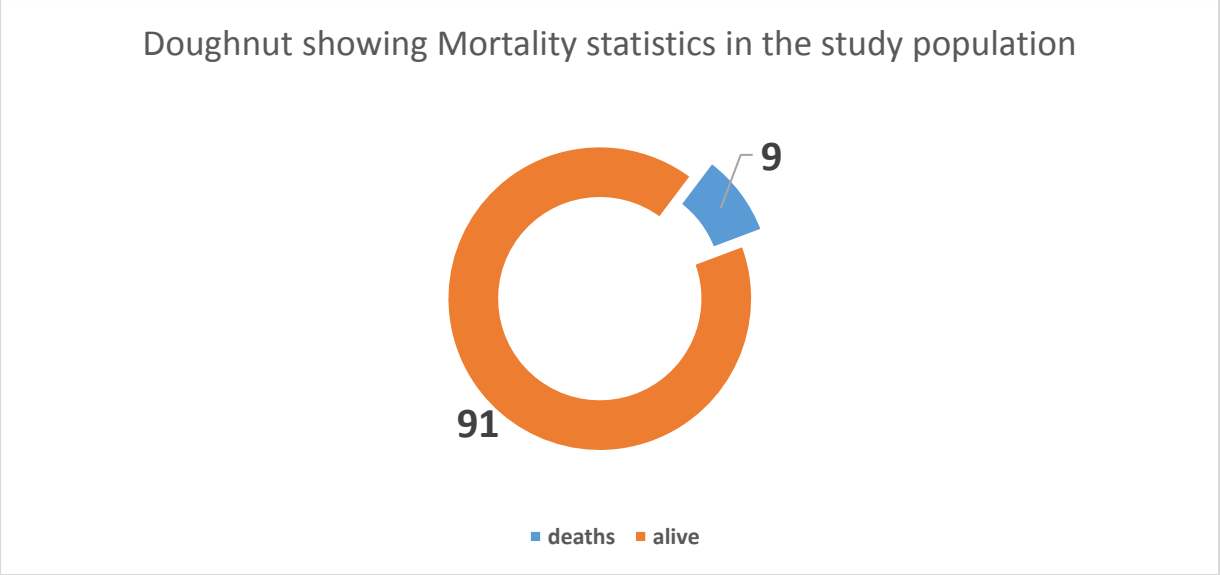


TABLE 14 : MORTALITY IN THE STUDY POPULATION

	Number of survived patients	Number of patients died (n)	Percentage of mortality (n %)
MALES	60	6	10%
FEMALES	31	3	9.68%

CHART 6 : BAR Graph GENDER DISTRIBUTION AND MORTALITY

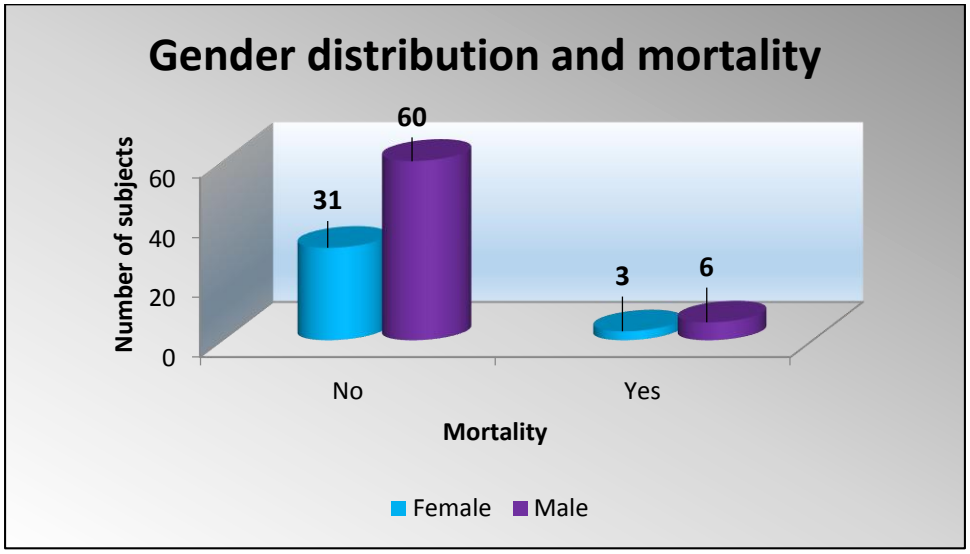
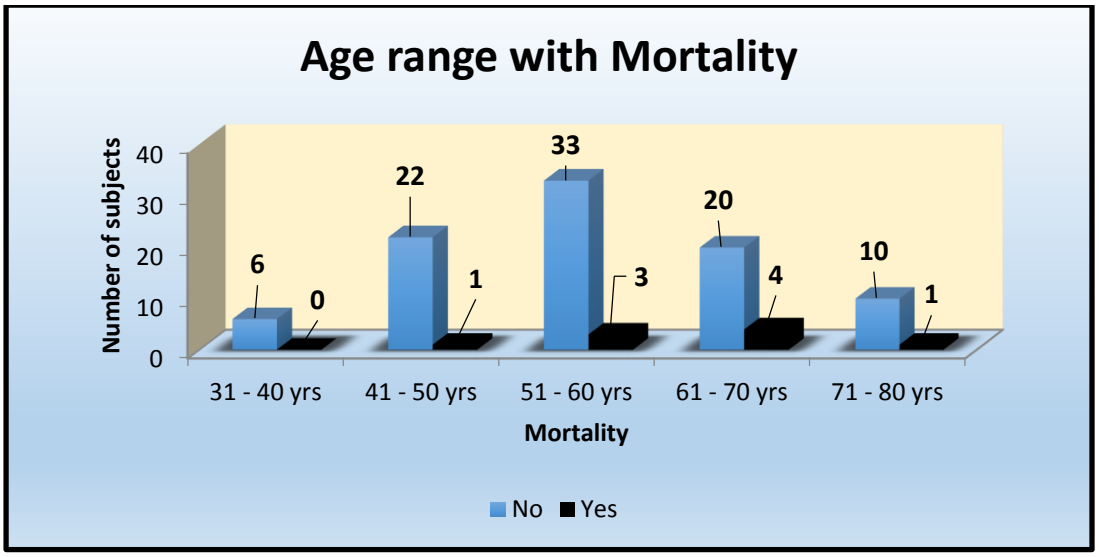


TABLE 15. AGE RANGE DISTRIBUTION WITH MORTALITY

		Mortality		
		No	Yes	Total
Agerange	31 - 40 yrs	6	0	6
	41 - 50 yrs	22	1	23
	51 - 60 yrs	33	3	36
	61 - 70 yrs	20	4	24
	71 - 80 yrs	10	1	11
Total		91	9	100

χ^2 value was 0.567 and the value was not statistically significant.

CHART 7 : BAR GRAPH showing AGE DISTRIBUTION WITH MORTALITY



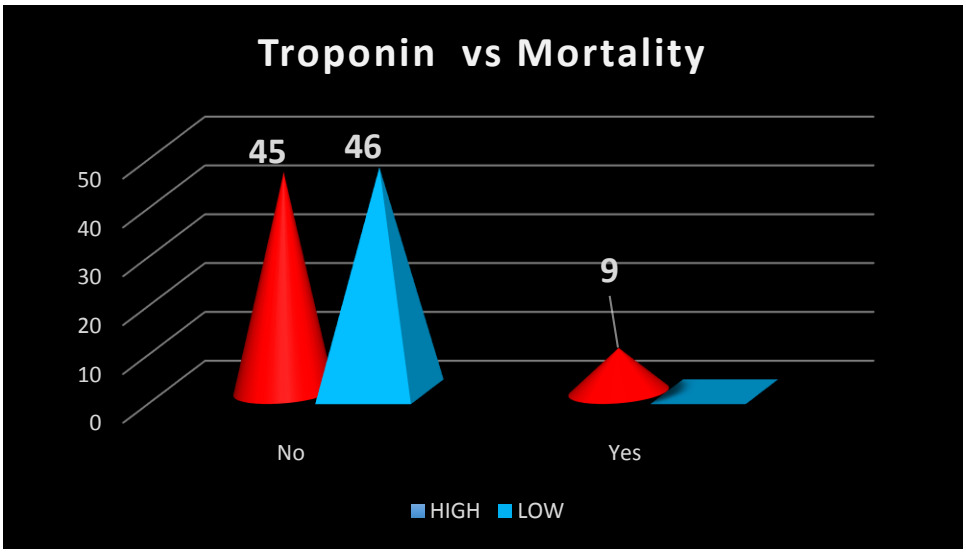
5. TROPONIN VALUE DISTRIBUTION

54 % of the study group had high levels of troponin and this high values were seen in all 9 cases of myocardial infarction that died. The **p value as per fisher's exact test was 0.003** indicating that the result is **statistically highly significant.**

TABLE 16 : TROPONIN ELEVATION WITH MORTALITY

		Mortality		
		No	Yes	Total
Troponin	HIGH	45	9	54
	LOW	46	0	46
Total		91	9	100

CHART 8: TROPONIN ASSOCIATION WITH MORTALITY



6. KILLIP CLASS and URIC ACID LEVEL DISTRIBUTION

TABLE 17 S. URIC ACID CORRELATION WITH KILLIP CLASS

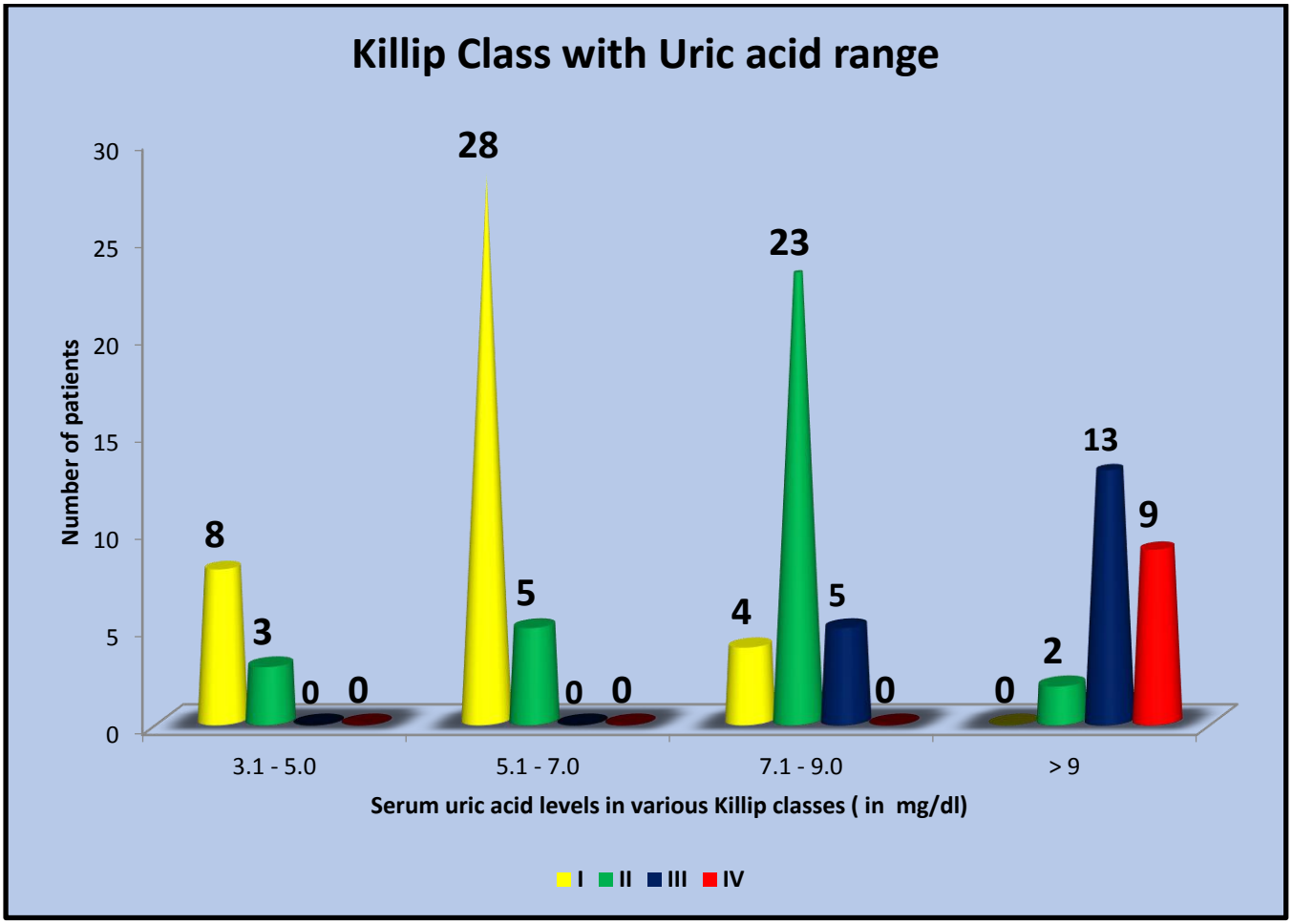
		Uric Acid Level (mg/dl)				Total
		3.1 - 5.0	**5.1 - 7.0**	**7.1 - 9.0**	**> 9**	
Killip Class	**I**	**8**	**28**	**4**	**0**	**40**
	II	**3**	**5**	**23**	**2**	**33**
	III	**0**	**0**	**5**	**13**	**18**
	IV	**0**	**0**	**0**	**9**	**9**
Total		**11**	**33**	**32**	**24**	**100**

40 patients belonged to killip class 1. 33 patients were in killip class 2 with 18 patients in killip class 3 and 9 patients in killip class 4 at the time of presentation.

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	111.525[a]	9	.0005
Likelihood Ratio	116.663	9	.000

CHART 9 - SERUM URIC ACID CORRELATION WITH KILLIP CLASS



24 patients had serum uric acid levels > 9mg/dl and 91.6 % belonged to killip classes 3 and 4.The **χ^2 value was 0.0005 and is thus highly significant statistically.**

7. HYPERURICEMIA and MORTALITY CORRELATION

The proportion of hyperuricemics in the study population was 59%.

Table 18 Showing Mortality Distribution According To S.Uric Acid Levels

		Mortality		
		No	Yes	Total
Uric acid levels	Normal	41	0	41
	Hyperuricemic	50	9	59
	Total	91	9	100

Chart 10 showing proportion of Hyperuricemia in study population

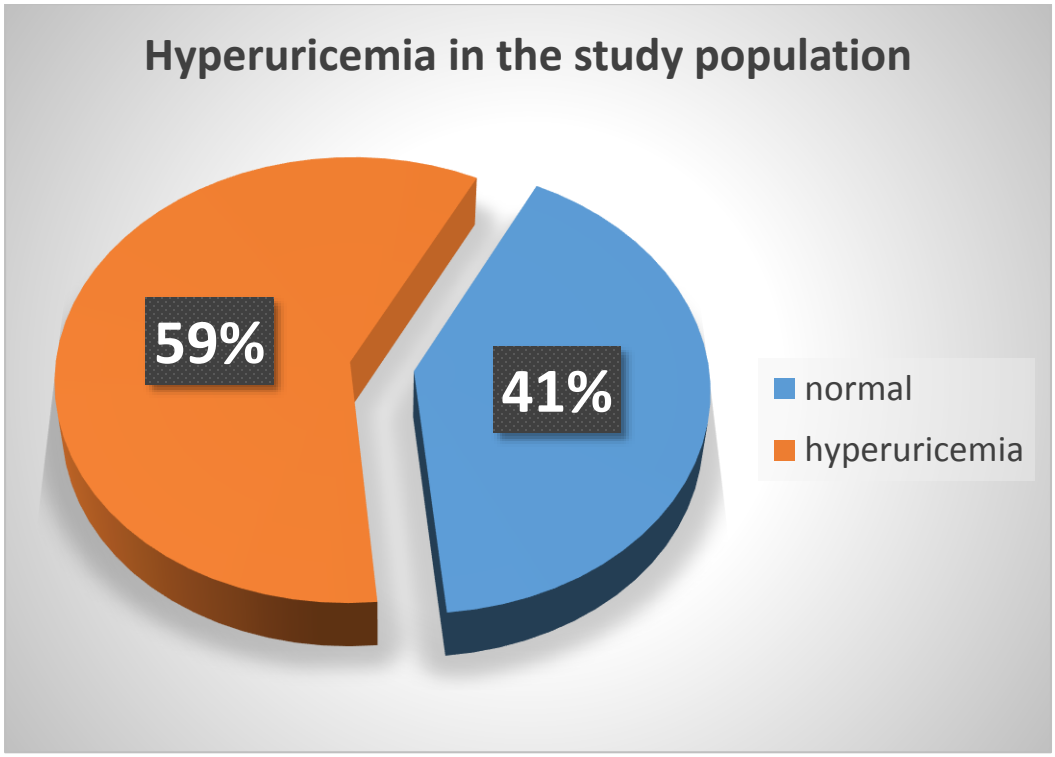
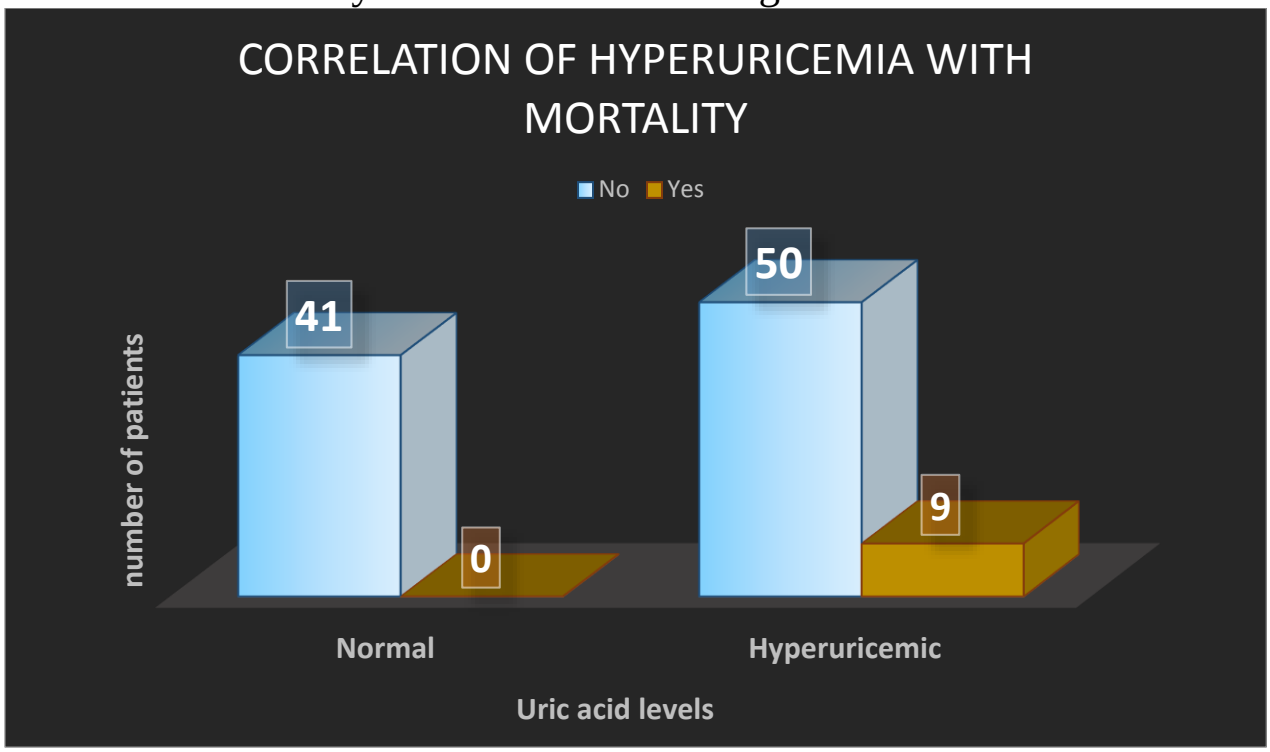


Chart 11 - Mortality Distribution According To S. Uric Acid Levels



The presence of hyperuricemia in the patients that died was 100%. 41% had normal serum uric acid levels and there were no deaths noted in the subgroup.

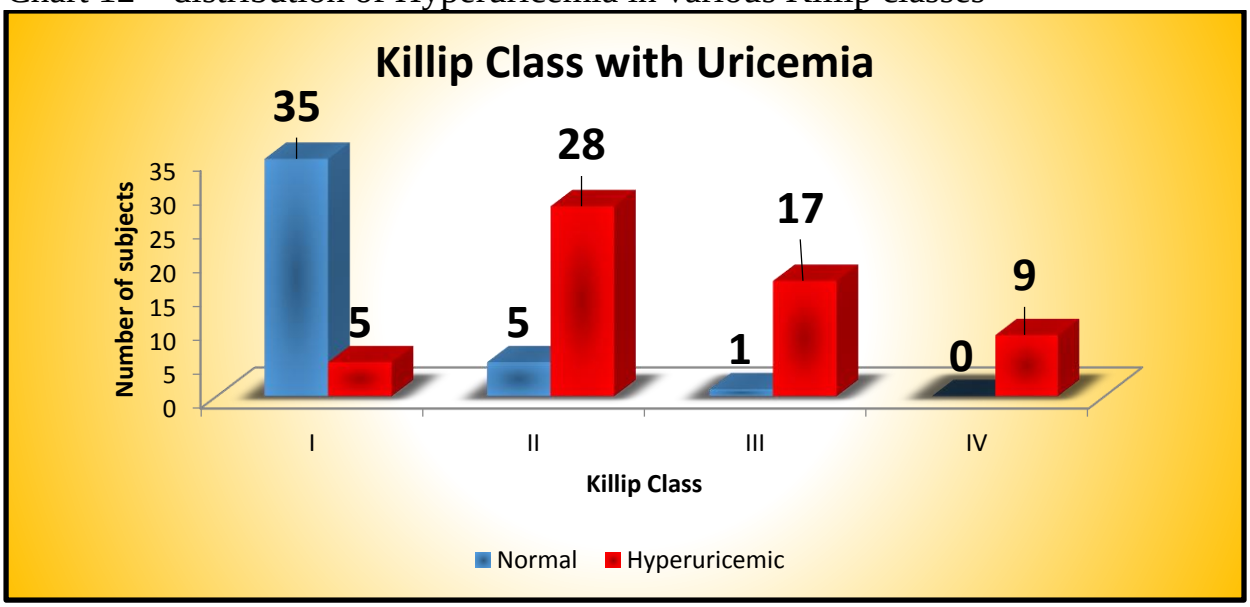
8. KILLIP CLASS DISTRIBUTION AND HYPERURICEMIA

Almost all individuals in Killip classes 3 and 4 had Hyperuricemia (96.3%)

Table 19 – distribution of Hyperuricemia in various Killip classes

		Serum Uric acid Level		
		Normal	Hyperuricemic	Total
Killip Class	I	35	5	40
	II	5	28	33
	III	1	17	18
	IV	0	9	9
Total		41	59	100

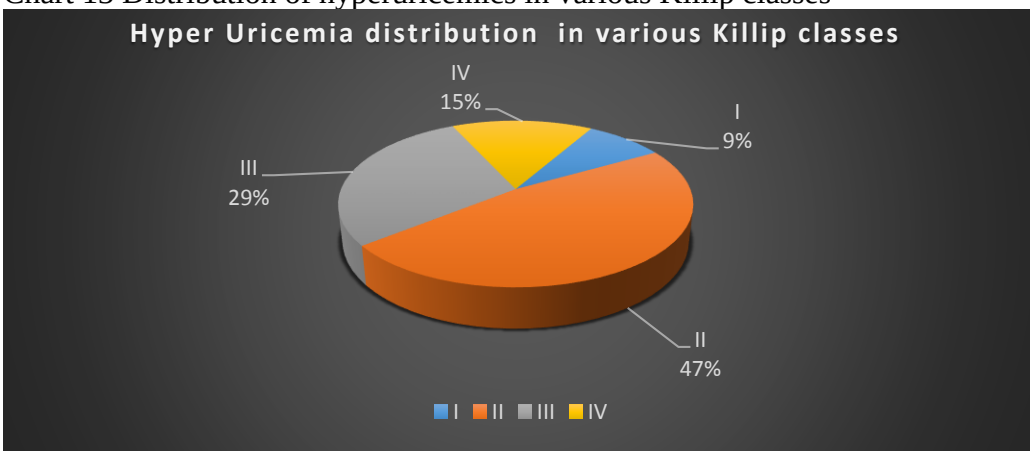
Chart 12 – distribution of Hyperuricemia in various Killip classes



	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	60.472[a]	3	.0005

The p value was 0.0005 indicating that the result is highly significant

Chart 13 Distribution of hyperuricemics in various Killip classes



Among the hyperuricemic individuals (n =59) , 5 belonged to killip class 1, 28 belonged to class II, 17 belonged to killip class 3 and 9 individuals were in killip class IV.

9. KILLIP CLASS AND MEAN SERUM URIC ACID LEVELS

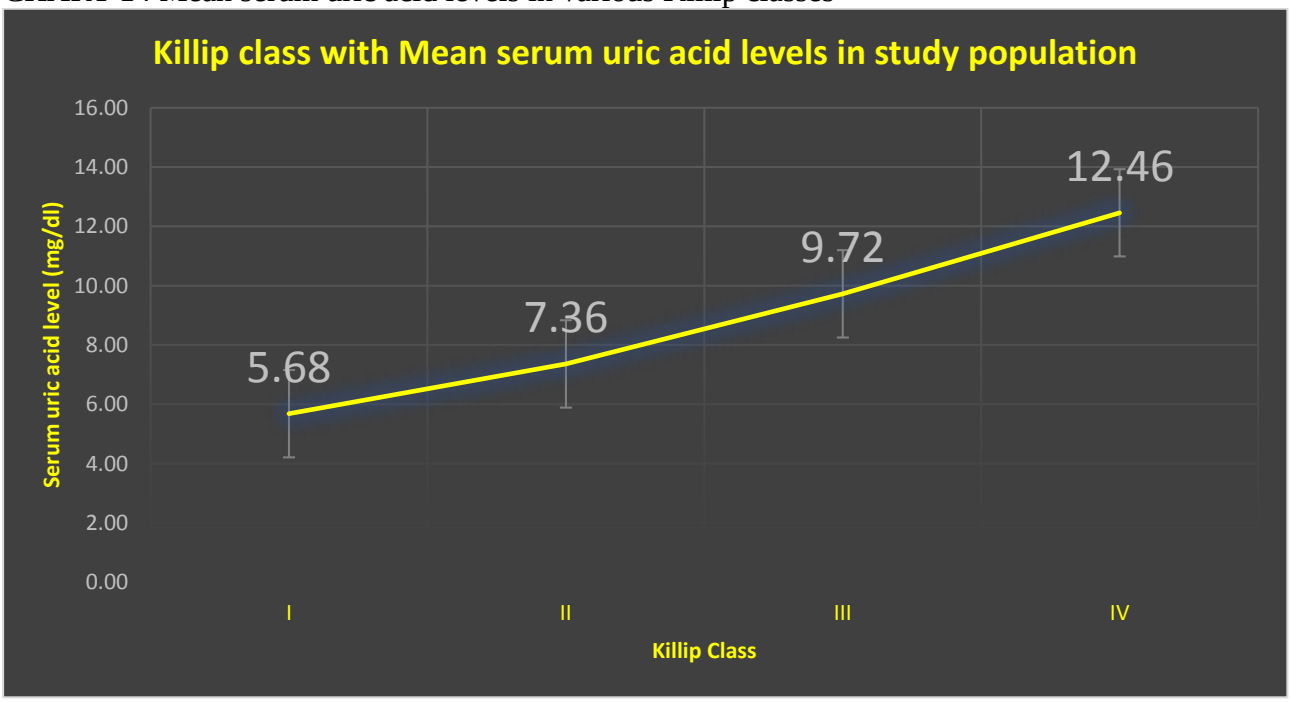
The Mean serum acid level in the study population was 7.57 +/- 2.31 mg/dl. Mean serum uric acid levels rose linearly with killip class. The mean serum uric level in killip classes 3 and 4 were 9.72 and 12.46 respectively. This indicates that serum uric acid levels correlated with the severity of myocardial infarction as assessed by killip classification. ANOVA test was utilized in the analysis and the **sigma value was 0.0005 indicating very high significance**.

Table 20 . Killip class and mean serum uric acid levels

Killip Class	Number of patients (n)	Mean Serum Uric Acid Levels	Standard Deviation	Standard. Error
I	40	5.68	0.96	0.15
II	33	7.36	1.11	0.19
III	18	9.72	0.85	0.20
IV	9	12.46	0.35	0.12
Total	100	**7.57**	**2.31**	0.23

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	442.525	3	147.508	158.832	.0005
Within Groups	89.156	96	.929		
Total	531.682	99			

CHART 14 Mean serum uric acid levels in various Killip classes



10. KILLIP CLASS and MEAN URIC ACID in HYPERURICEMIA

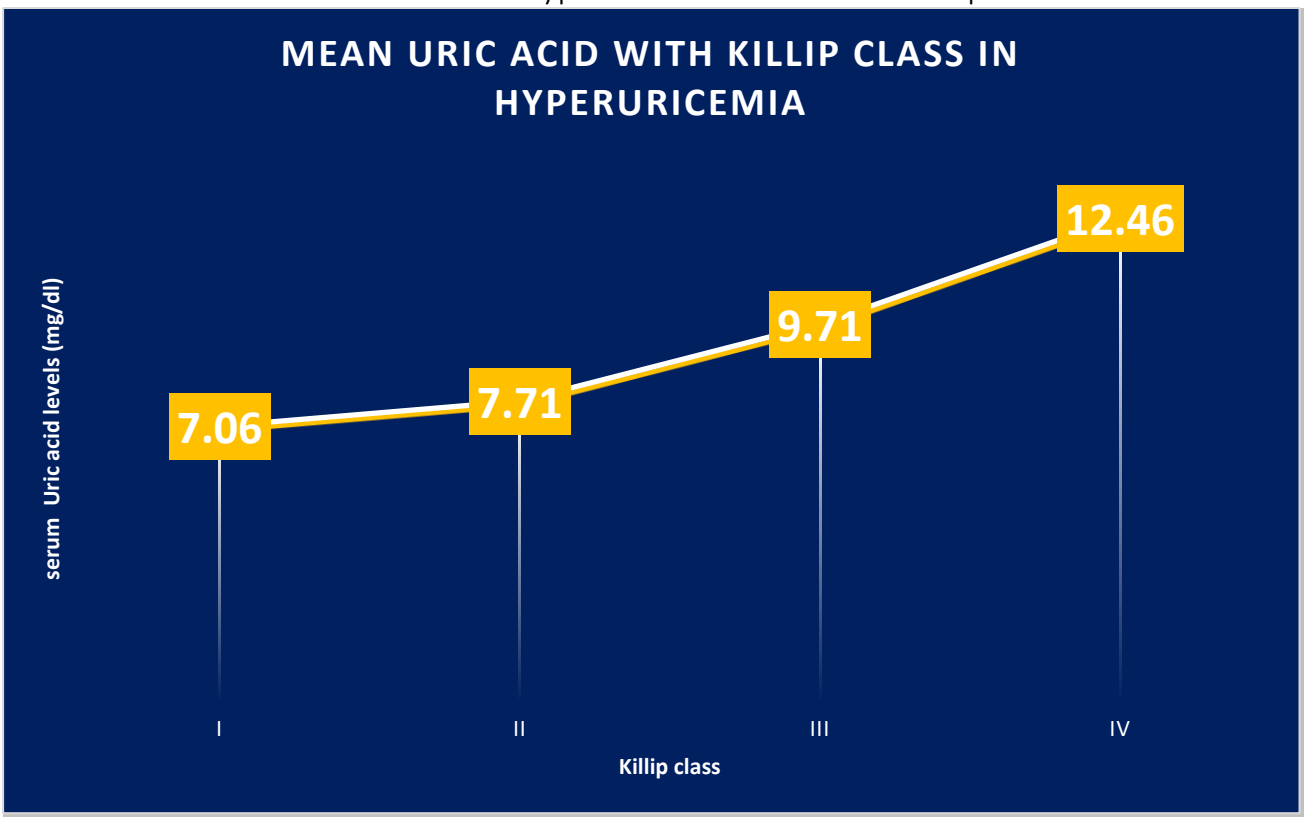
The mean uric acid levels in hyperuricemic individuals is 8.96 +/-1.9 mg/dl. The mean serum acid levels in the entire study population was 7.57+/-2.5 mg/dl. Similar linear progression of increase in uric acid levels were noted in the hyperuricemia sub group also. ANOVA test was utilized in the analysis and the values were **statistically highly significant**.

Table 21 : Mean serum acid in hyperuricemics of various Killip classes

Killip Class of the individual	Number of hyperuricemics (n)	Mean	Std. Deviation	Std. Error
I	5	7.06	0.43	0.19
II	28	7.71	0.64	0.12
III	17	9.71	0.88	0.21
IV	9	12.46	0.35	0.12
Total	59	8.96	1.88	0.24

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	181.327	3	60.442	132.874	.0005
Within Groups	25.019	55	.455		
Total	206.345	58			

Chart 15 : Mean Mean serum acid in hyperuricemics of various Killip classes



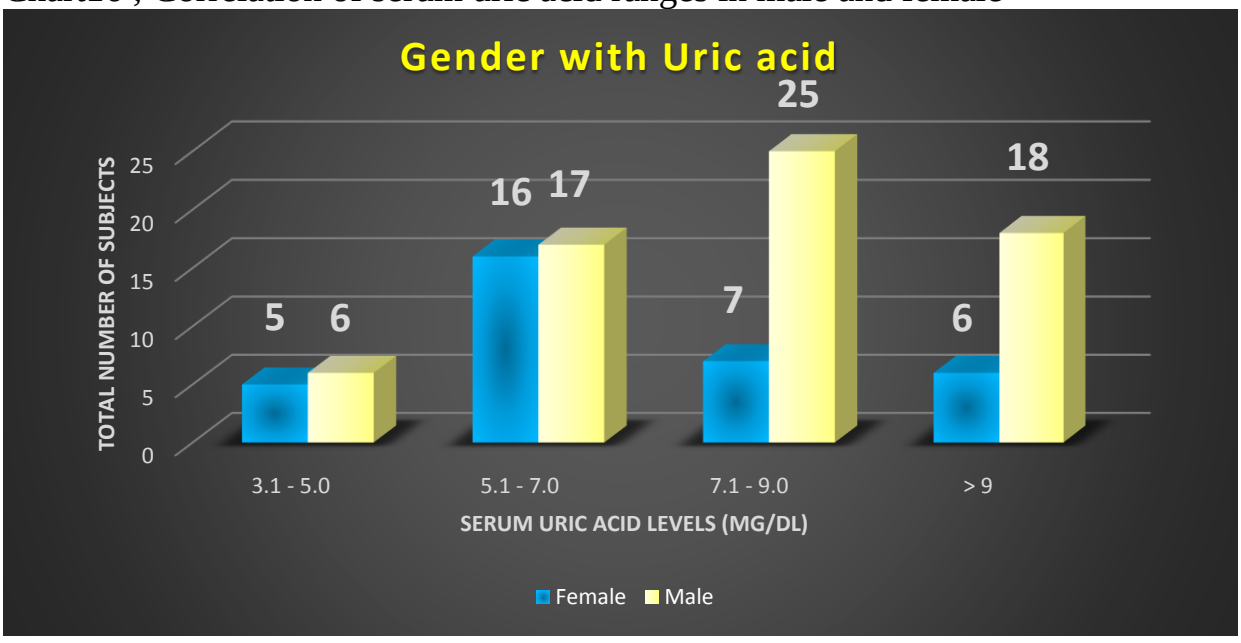
11. SERUM URIC ACID LEVELS WITH GENDER CORRELATION

There was no correlation serum uric acid in various age groups in either genders

Table 22 ; Correlation of serum uric acid ranges in male and female

		Serum Uric acid level (mg/dl)				
		3.1 - 5.0	5.1 - 7.0	7.1 - 9.0	> 9	Total
Sex	Female	5	16	7	6	34
	Male	6	17	25	18	66
Total		11	33	32	24	100

Chart16 ; Correlation of serum uric acid ranges in male and female



χ^2 test was applied for analysis and p values was 0.082 and was not statistically significant.

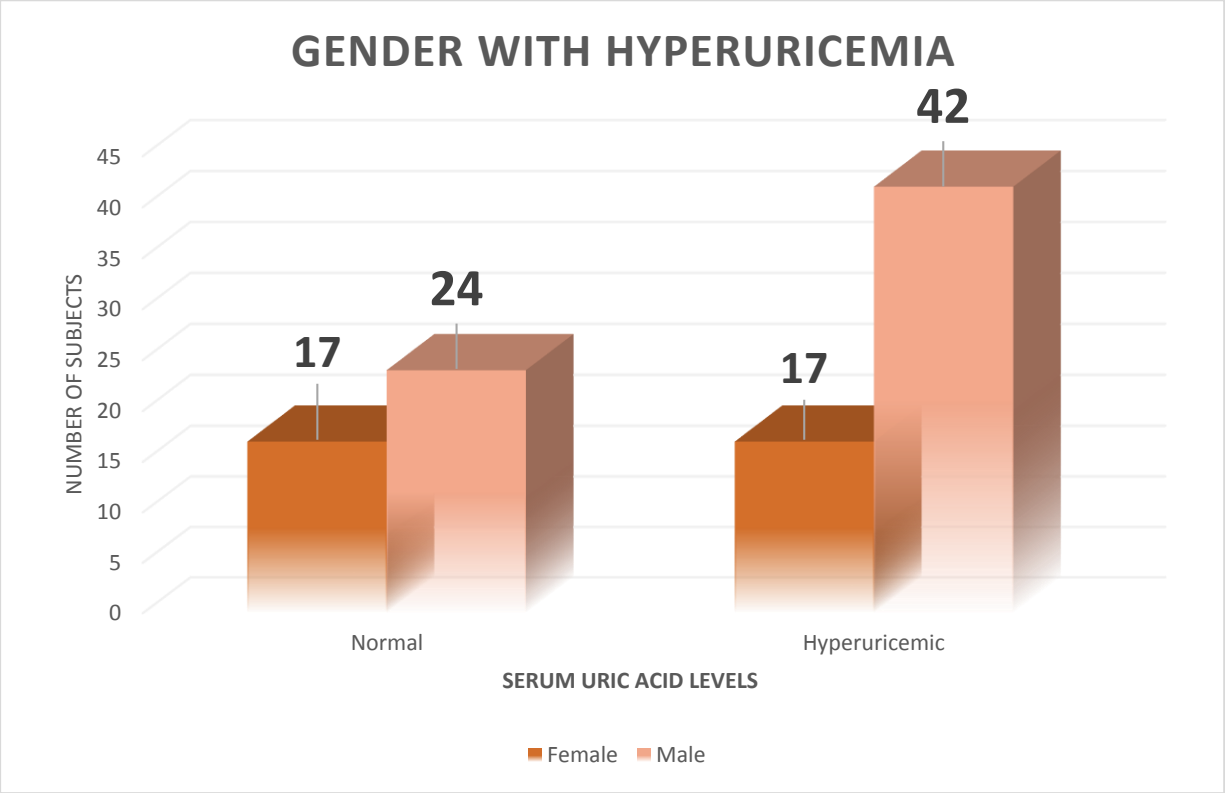
12. HYPERURICEMIA STATUS and GENDER DISTRIBUTION

50 % of the females in the study population had hyperuricemia defined as serum uric acid levels more than 6 mg/dl. 63.6% of the males in the study population had hyperuricemia defined as serum uric acid levels more than 7mg/dl. The chi square test was applied and p value was 0.189 and is not statistically significant.

Table 23 : Gender and serum uric acid distribution

		Serum Uric acid levels		
		Normal	Hyperuricemic	Total
Sex	Female	17	17	34
	Male	24	42	66
Total		41	59	100

Chart 17 : Gender and serum uric acid distribution



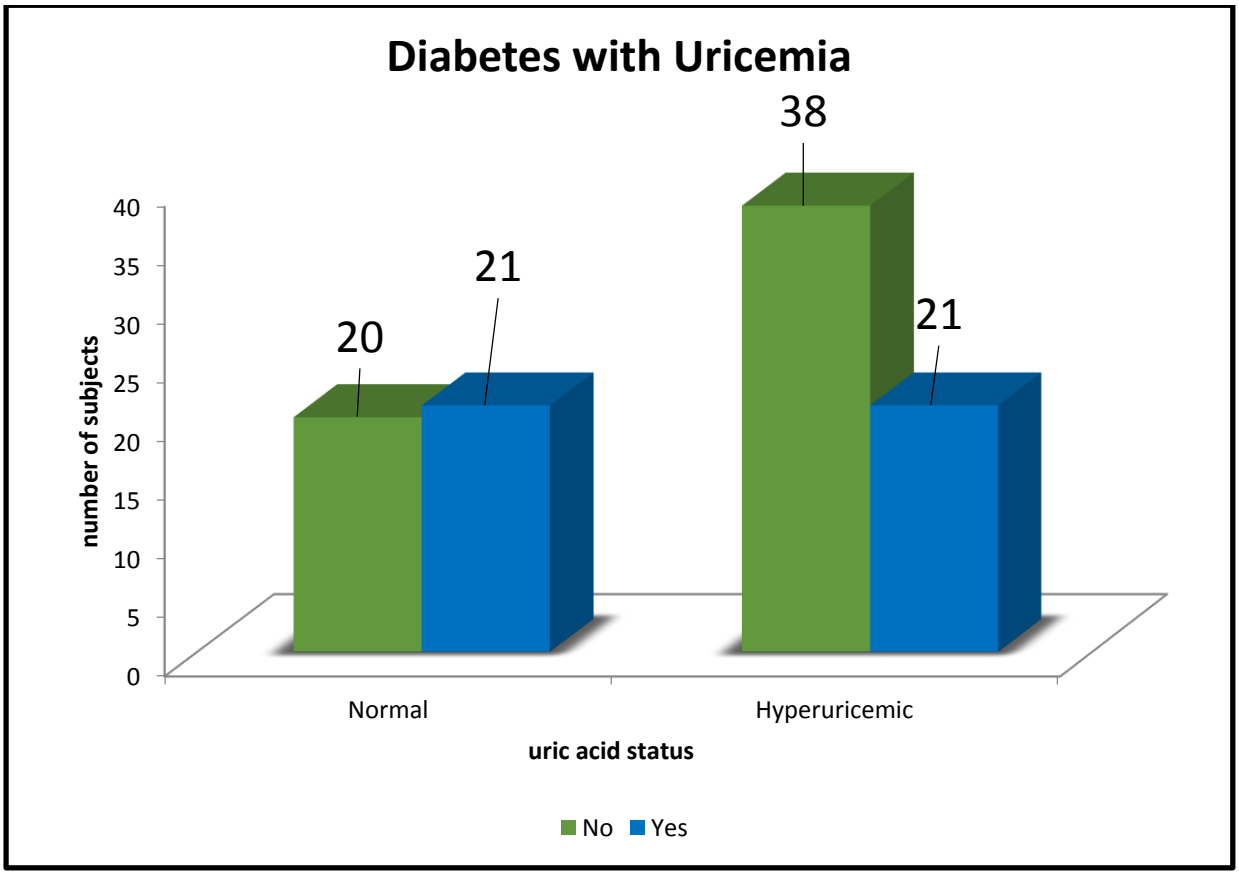
13. DIABETES AND URIC ACID

There were 42 individuals with type 2 diabetes mellitus in the study group and the proportion of Hyperuricemics noted in the diabetic sub group was 50%. **χ^2 value was 2.425 and p value 0.119. This is not statistically significant**

Table 24 : Distribution of serum uric acid levels in diabetics and non diabetics

		Serum Uric acid level		
		Normal	Hyperuricemic	Total
DIABETES	No	20	38	58
	Yes	21	21	42
Total		41	59	100

Chart 18 Distribution of serum uric acid levels in diabetics and non diabetics



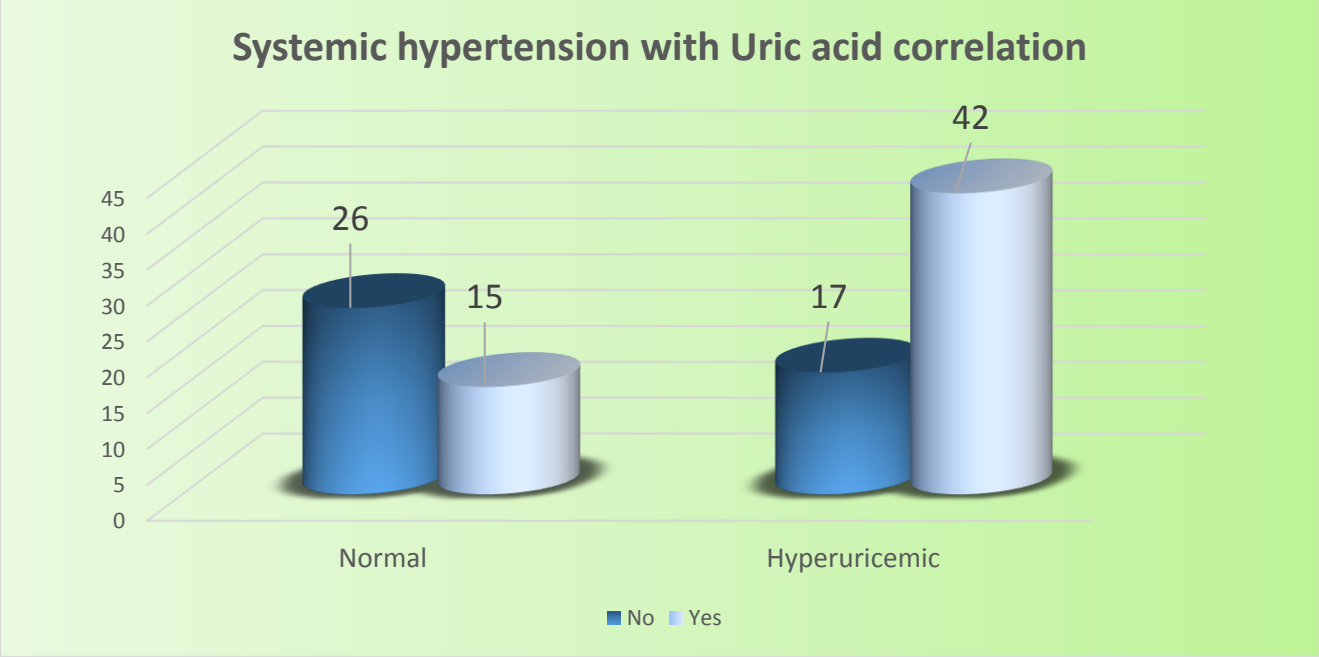
14. HYPERTENSION AND URIC ACID

57 patients were hypertensives and 43 patients were non hypertensives. The incidence of Hyperuricemia in hypertensives was 73%. On applying χ^2 test, the p value was 0.001 indicating that the association has high statistical significance.

Table 25 : Distribution of serum uric acid levels in HT and Non HTives

		serum uric acid		
		Normal	Hyperuricemia	Total
HTN	No	26	17	43
	Yes	15	42	57
Total		41	59	100

Chart 19 : Distribution of serum uric acid levels in HT and Non HTives



15. SMOKING and URIC ACID

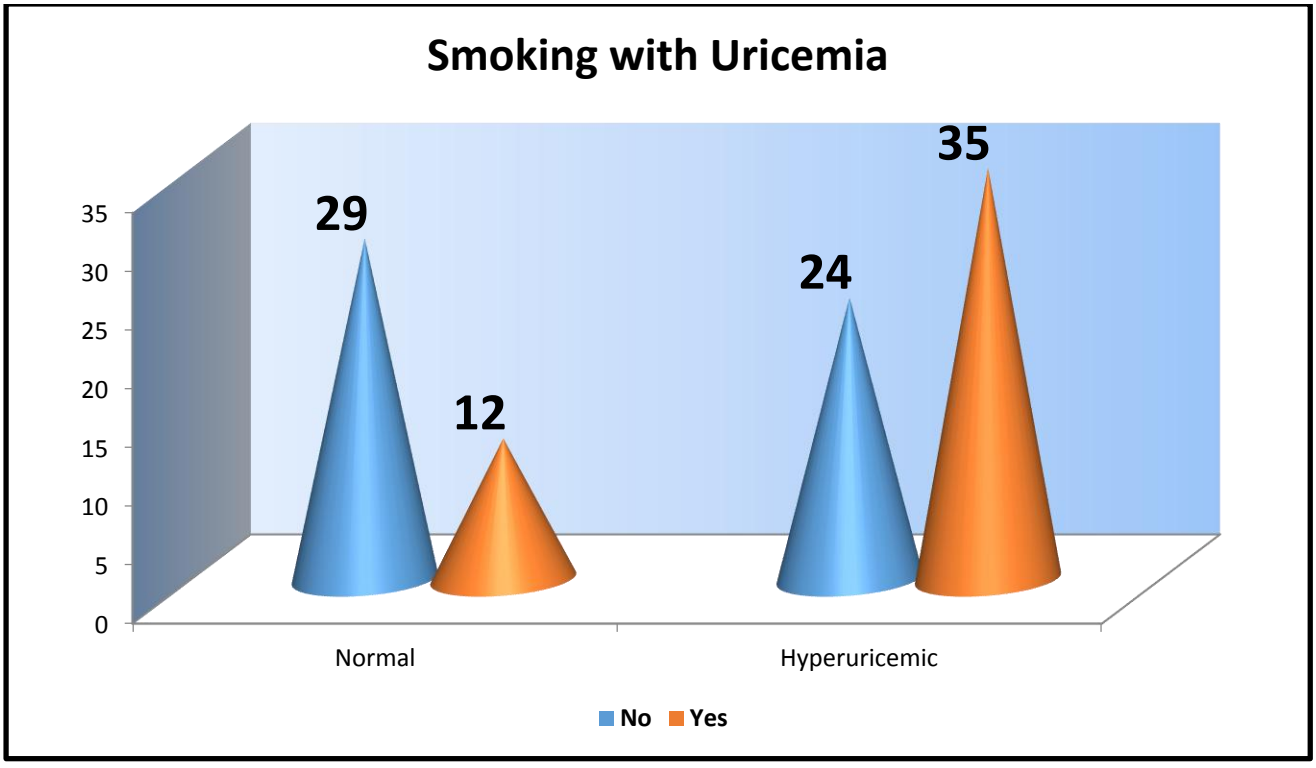
47 out of 100 patients were smokers. 35 of them had Hyperuricemia (74.47%). There is a significant association between smoking and Hyperuricemia (p value 0.003).

Table 26 : Distribution of serum uric acid levels in smokers and non smokers

		Serum uric acid		
		Normal	Hyperuricemic	Total
SMOKING	No	29	24	53
	Yes	12	35	47
Total		41	59	100

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.771[a]	1	.003

Chart 20 : Distribution of serum uric acid levels in smokers and non smokers



16. SERUM CHOLESTEROL with URIC ACID

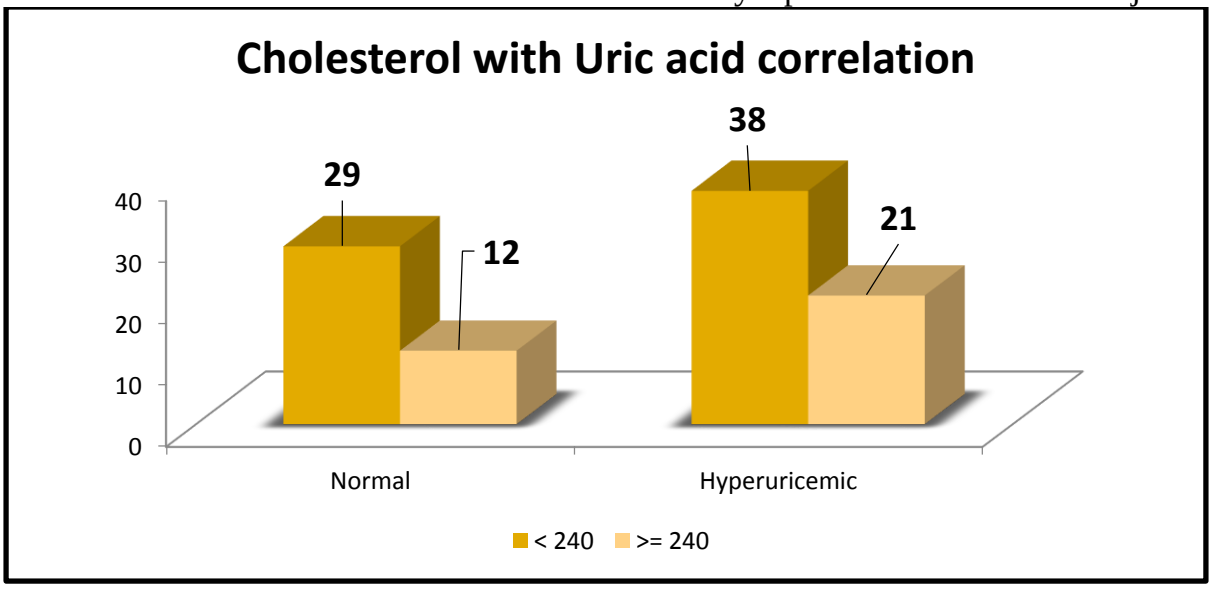
33 out of the 100 patients had hypercholesterolemia. 21 out of the 33 dyslipidemic subgroup had Hyperuricemia (63.6%) but the association is not statistically significant. (p value 0.508)

Table 27 : Distribution of serum uric acid levels in dyslipidemics and normal subjects

		Serum uric acid		
		Normal	**Hyper uricemic**	**Total**
Cholesterol range	**< 240**	**29**	**38**	**67**
	≥240	**12**	**21**	**33**
Total		**41**	**59**	**100**

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.438[a]	1	.508

Chart 21: Distribution of serum uric acid levels in dyslipidemics and normal subjects



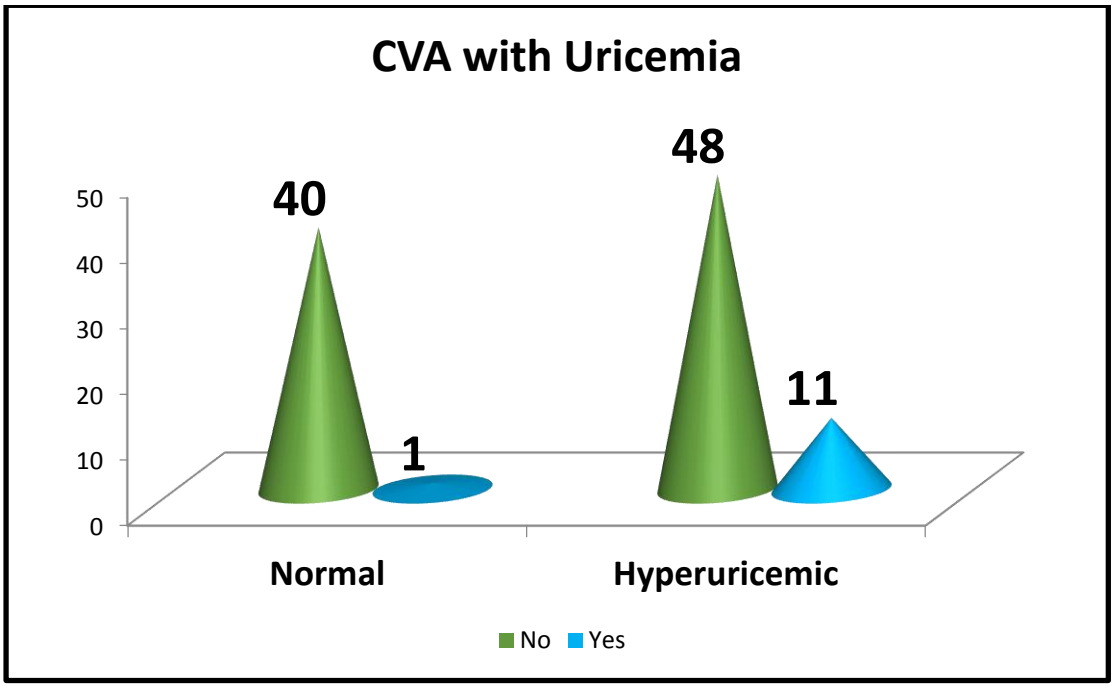
17. URIC ACID and PRIOR CEREBRO VASCULAR DISEASE

12 out of the 100 cases had a past history of cerebro vascular accident. 11 out of the 12 cases (91.67%) had Hyperuricemia. The association between Hyperuricemia and cerebrovascular disease was found to be statistically significant. (p value 0.025)

Table 28 : Distribution of serum uric acid levels in subjects with prior CVA

		Serum Uric Acid status		
		Normal	Hyperuricemic	Total
CVA	No	40	48	88
	Yes	1	11	12
Total		41	59	100

Chart 22 : Distribution of serum uric acid levels in subjects with prior CVA



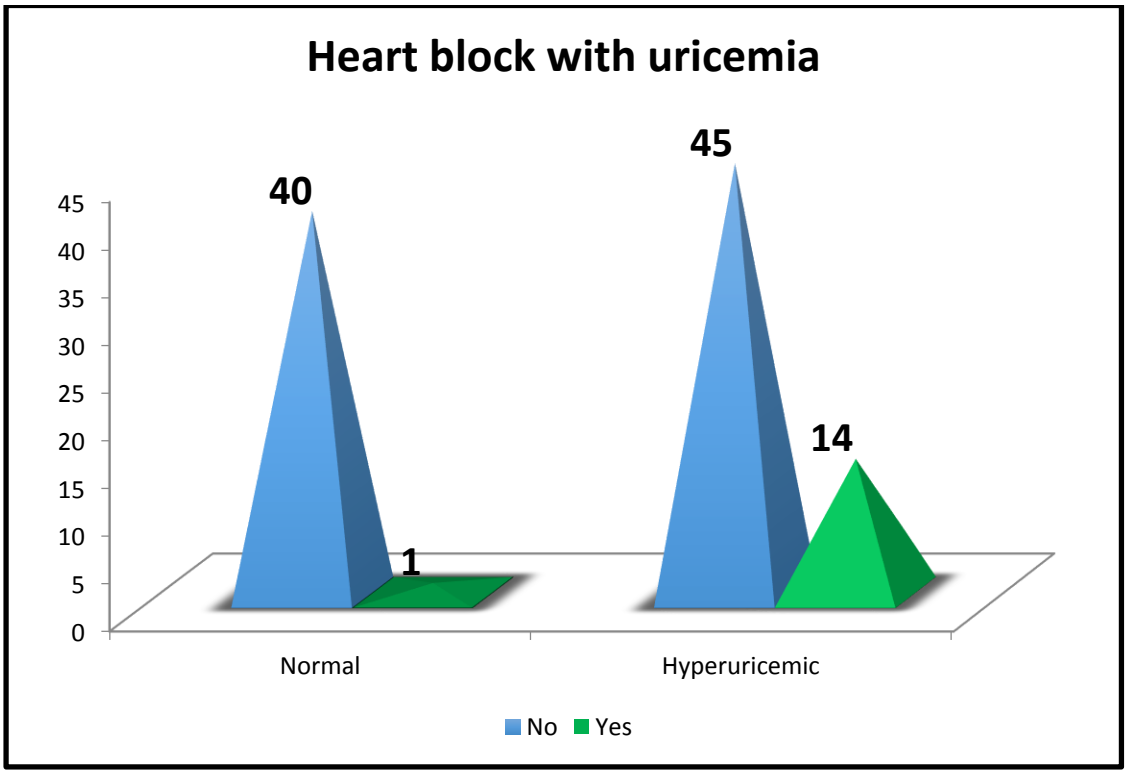
18. HYPERURICEMIA and HEART BLOCKS

15 out of the 100 cases of myocardial infarction had heart blocks. 14 out of the 15 cases were noted to have Hyperuricemia (93.34%). Significant association was noted between incidence of heart blocks and Hyperuricemia (p value 0.003).

Table 29 : Distribution of serum uric acid levels in subjects with heart block

		Uricemia status		
		Normal	Hyperuricemic	Total
Heart Block	No	40	45	85
	Yes	1	14	15
Total		41	59	100

Chart 23 : Distribution of serum uric acid levels in subjects with heart block



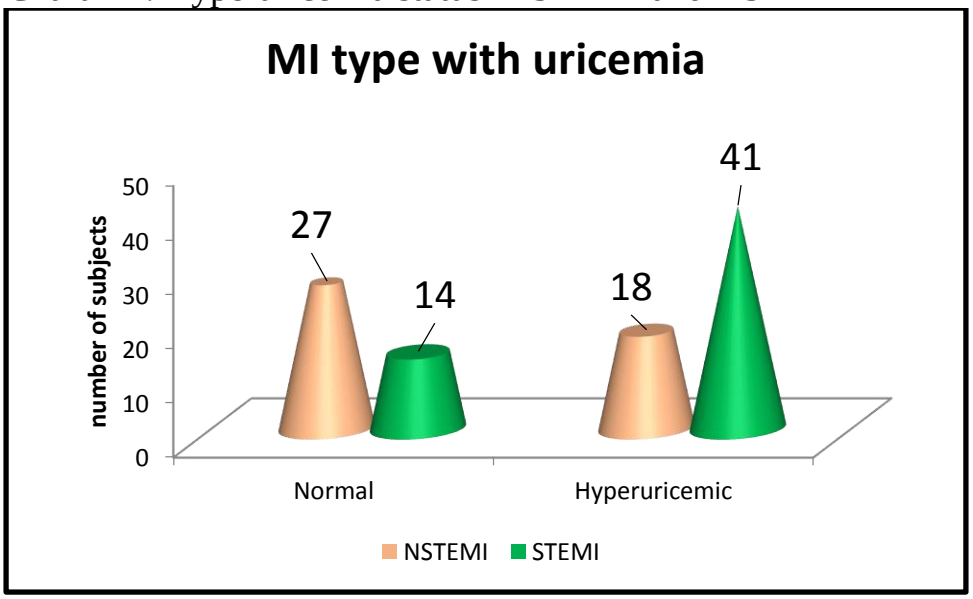
19. HYPERURICEMIA AND TYPE OF MYOCARDIAL INFARCTION

Out of the 59 cases who had hyper uricemia, 41 cases had ST elevation MI and 18 cases had Non ST elevation MI. There was a statistically significant association between Hyperuricemia and STEMI (p value <0.005). ie. 74.5% of subjects with STEMI had Hyperuricemia whereas it is only 40% in subjects with NSTEMI.

Table 30 : Hyperuricemia status in STEMI and NSTEMI

TYPE OF MI	Hyperuricemia cases (n)	Total Cases	Percentage (n%)
STEMI	**41**	**55**	**74.5%**
NSTEMI	**18**	**45**	**40%**
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	12.210[a]	1	.0005

Chart 24 : Hyperuricemia status in STEMI and NSTEMI



20. MYOCARDIAL INFARCTION LOCATIONS AND SERUM URIC ACID

Out of the 100 cases, 27 cases had antero-septal wall MI, 44 cases had anterior wall myocardial infarction. 25 cases were inferior wall MI and 3 cases suffered from infero posterior wall MI with 1 case of inferoposterior all with right ventricular MI.

Hyperuricemia was noted in 17 out of 27 cases of anteroseptal MI (63%), 28 out of 44 cases of anterior all MI (63.7%), 8 out of 25 cases of inferior wall MI (32%) and 3 out of 4 cases of inferoposterior with right ventricular MI (75%). The net incidence of Hyperuricemia in inferior wall related myocardial infarction was 28.2%.(11 out of 29 cases). The association of higher serum uric acid levels in majority of anterior wall myocardial infarction cases was not found to have statistic significance (p value 0.162)

Table 31 : distribution of uric acid in various MI

Location of infarction	serum uric acid (mg/dl)				Total
	3.1 - 5.0	5.1 - 7.0	7.1 - 9.0	> 9	
AS	2	8	9	8	27
AW	5	11	17	11	44
IW	4	13	6	2	25
IW+PW	0	0	0	1	1
IW+PW+RV	0	1	0	2	3
Total	11	33	32	24	100

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	20.264a	15	.162
Likelihood Ratio	20.078	15	.169

Chart 25 : Distribution of MI Locations in study population

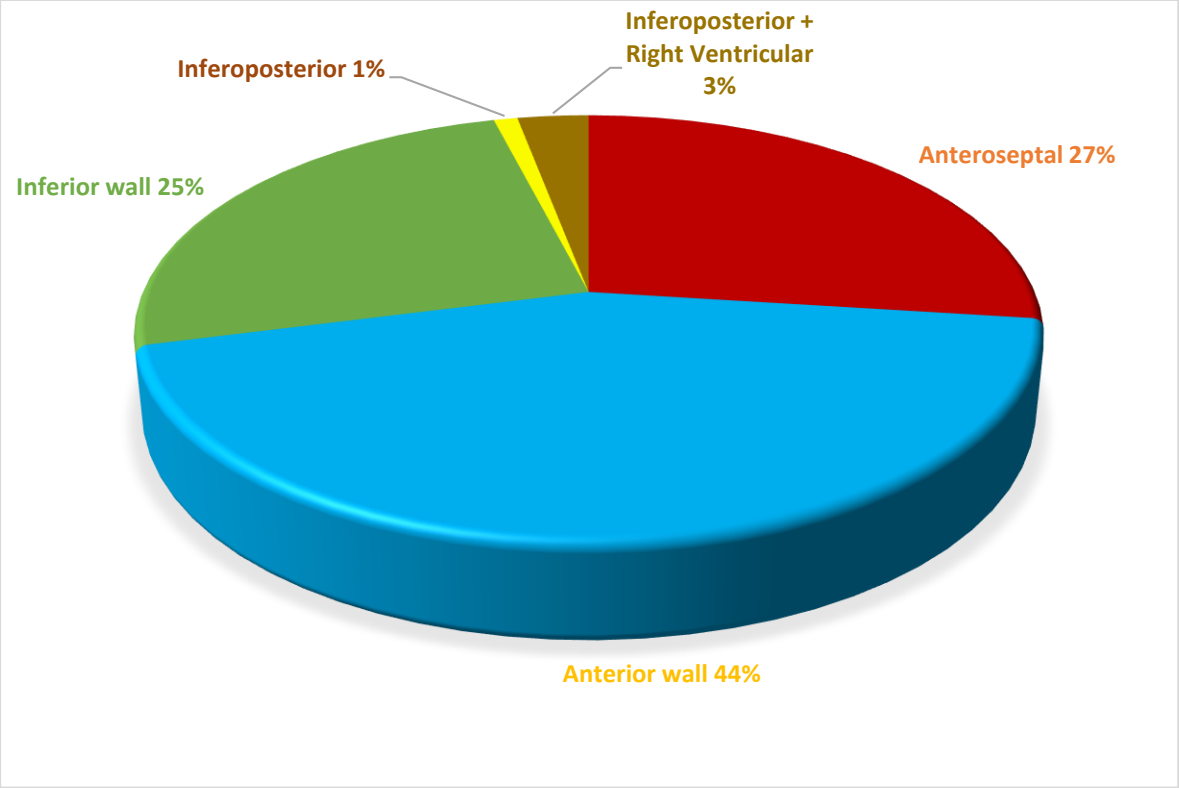


Chart 26 : Distribution of Hyperuricemia in various MI subtypes

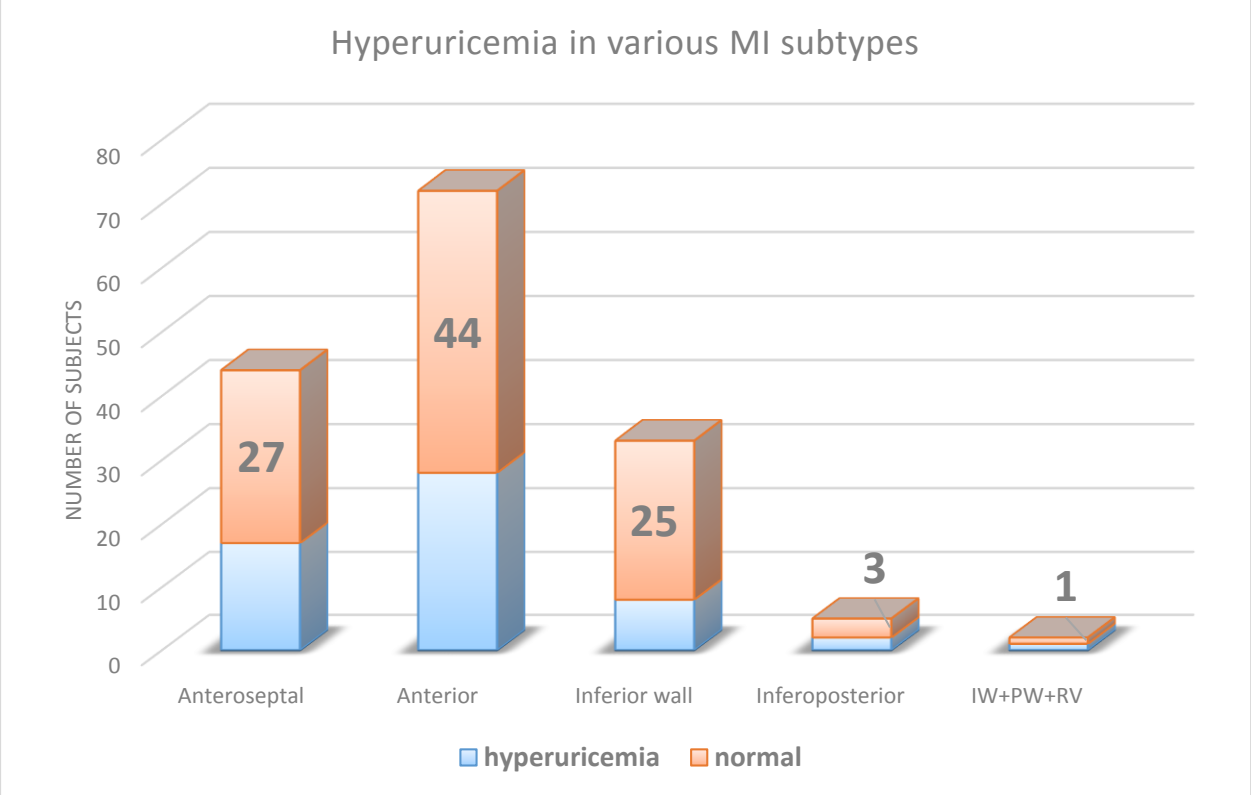
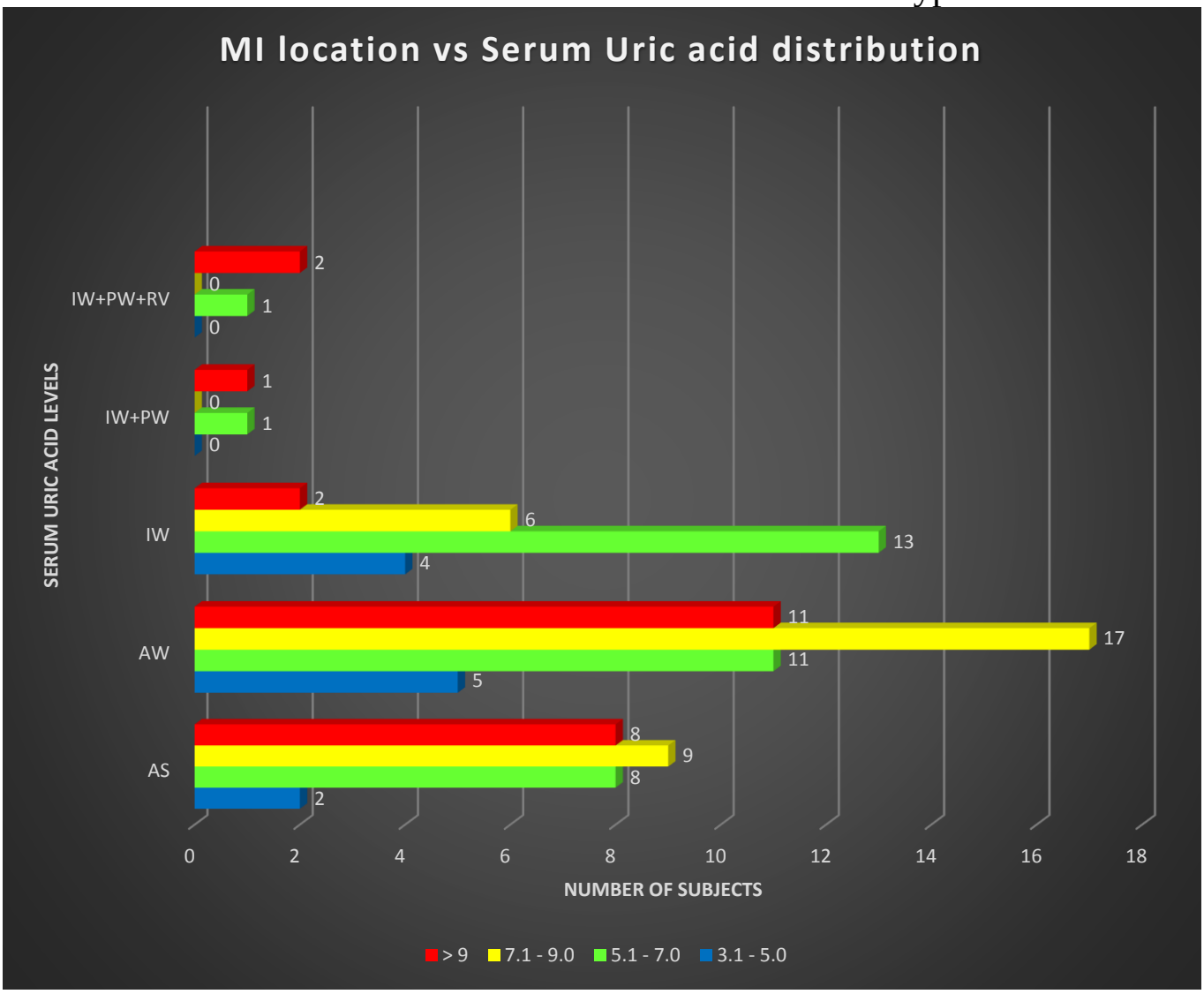


Chart 27 : Distribution of serum uric acid in various MI subtypes



Higher serum uric acid levels were seen in cases of anterior wall and anteroseptal wall myocardial infarction cases as compared to inferior wall and inferoposterior wall myocardial infarction cases and the association did not have statistical significance. The number of inferoposterior wall myocardial infarction cases were less as compared to the anterior wall MI cases. Hence significant analysis could not be made.

21. SERUM URIC ACID and TYPE OF MI

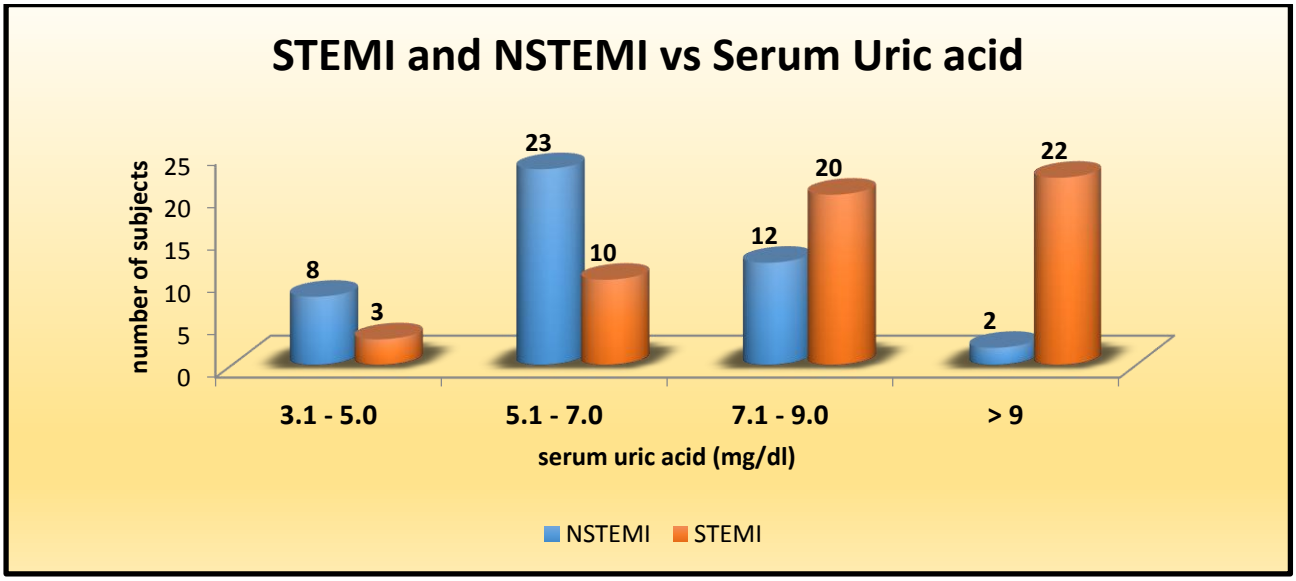
The overall proportion of Hyperuricemia was more in subgroups with STEMI and NSTEMI and the association was statistically significant.

Table 32 : Serum Uric acid distribution in STEMI and NSTEMI

		serum uric acid (mg/dl)				
		3.1 - 5.0	5.1 - 7.0	7.1 - 9.0	> 9.0	Total
MI Type	NSTEMI	8	23	12	2	45
	STEMI	3	10	20	22	55
Total		11	33	32	24	100

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	25.314[a]	3	.0005
Likelihood Ratio	28.144	3	.000

Chart 28 : Serum Uric acid distribution in STEMI and NSTEMI

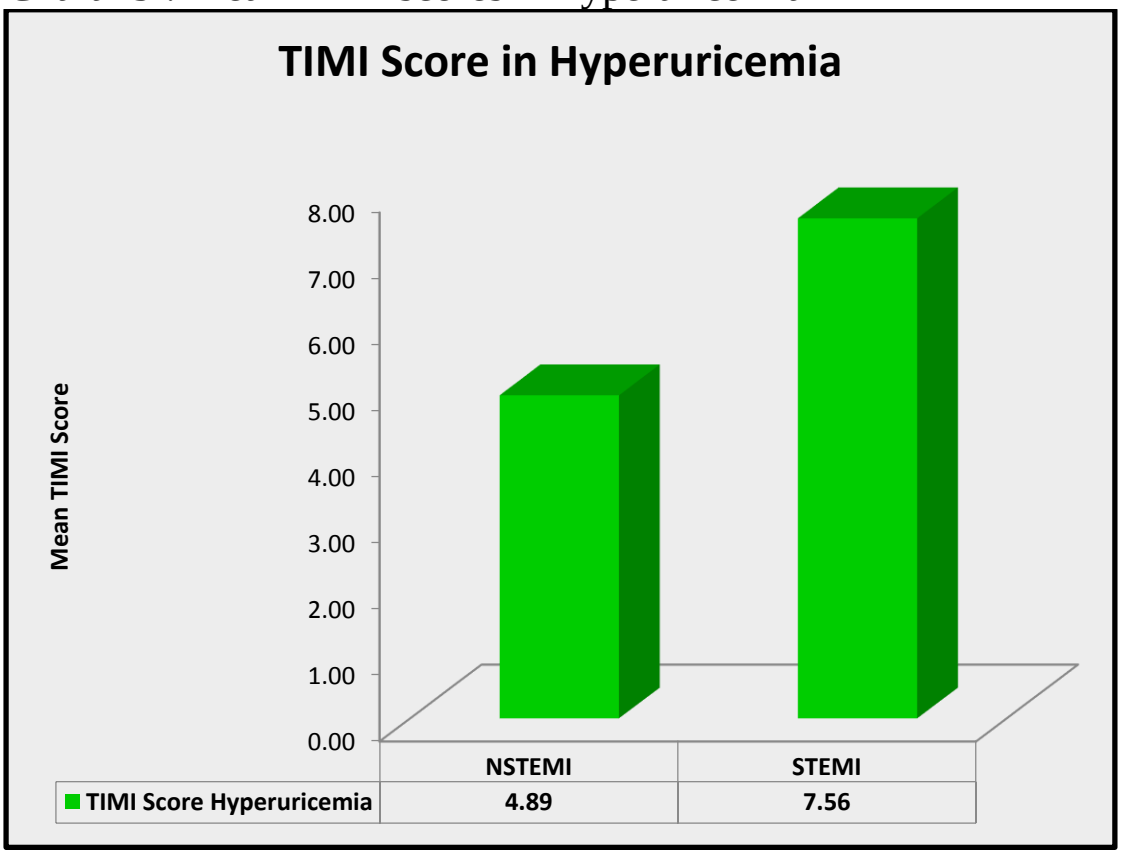


22. **URIC ACID and TIMI SCORE**

The mean TIMI score in hyperuricemic subjects in NSTEMI cases was 4.89 ± 0.9 and 7.56±2.5 in cases of STEMI.

	NSTEMI (max score 7)	STEMI (max score 13)
Mean TIMI Score	4.89 ± 0.9	7.56 ± 2.5

Chart 29 : Mean TIMI scores in hyperuricemia



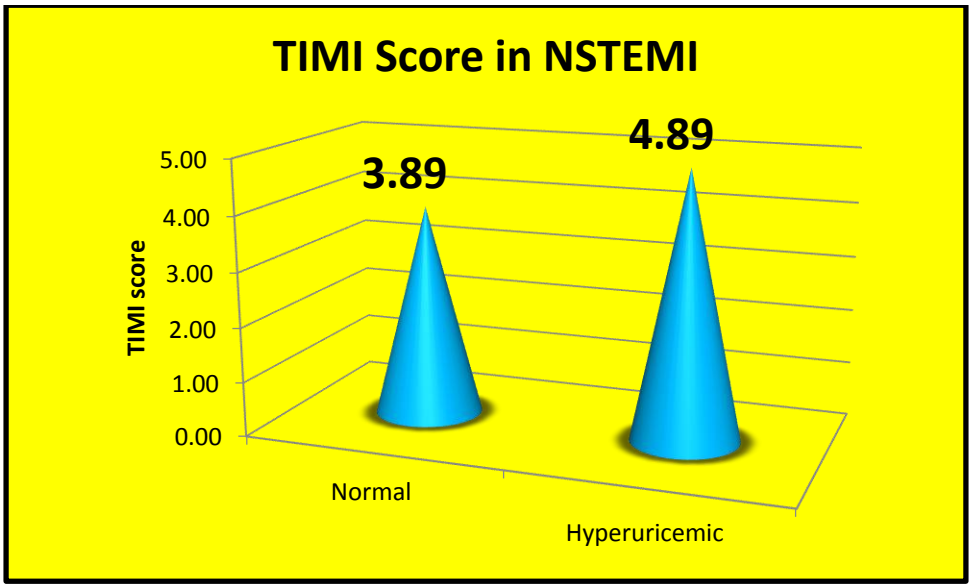
23. TIMI score in NSTEMI and SERUM URIC ACID

The mean TIMI score in NSTEMI subgroup with normal uric acid levels were 3.89 whereas it is 4.89 in the subgroup of NSTEMI with Hyperuricemia. **The t test was applied for the 2 independent variables and the result was statistically significant. (p value 0.0005)**

Table 33 : Serum uric acid and TIMI score in NSTEMI

Serum Uric acid status		N	Mean	Std. Deviation	Std. Erro
TIMI SCORE	Normal	27	3.89	0.8	0.15
	Hyperuricemic	18	4.89	0.9	0.21

Chart 30 : Serum uric acid and TIMI score in NSTEMI



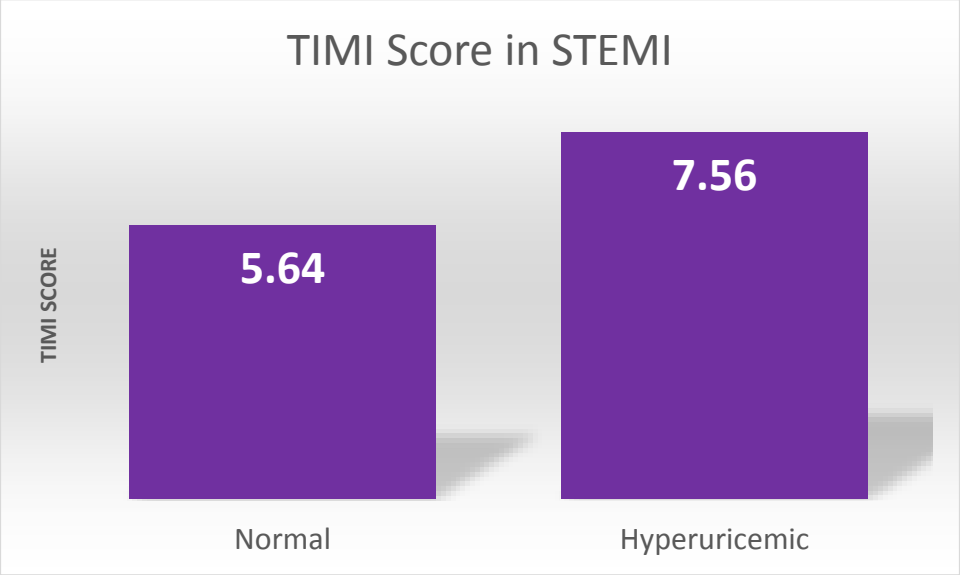
24. TIMI score in STEMI and SERUM URIC ACID

The mean TIMI score in STEMI subgroup with normal uric acid levels were 5.64±2.3 whereas it was 7.56±2.5 in the subgroup of STEMI with Hyperuricemia. The mean TIMI score was higher in the Hyperuricemia subgroup in STEMI. **The t test was applied for the 2 independent variables and the result was statistically significant. (p value 0.0016)**

Table 34 : Serum uric acid and TIMI score in STEMI

Serum uric acid status		N	Mean	Std. Deviation	Std. Error
TIMI SCORE	Normal	14	5.64	2.3	0.6
	Hyperuricemic	41	7.56	2.5	0.4

Chart 31 : Serum uric acid and TIMI score in STEMI



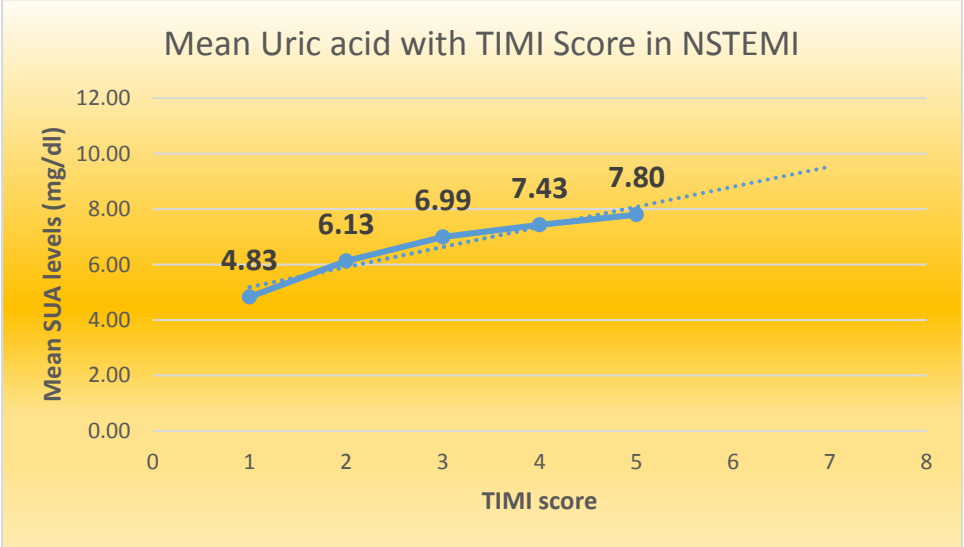
25. MEAN SERUM URIC ACID and TIMI SCORE in NSTEMI

As the graph depicts, a linear increase in mean serum uric acid levels were noted in patients with higher TIMI scores in NSTEMI.

Table 35 : Serum uric acid distribution for TIMI score in NSTEMI

	Serum uric acid (mg/dl)		
TIMI Score	N	Mean	Std. Deviation
3	10	4.83	0.85
4	17	6.13	1.13
5	14	6.99	1.32
6	3	7.43	0.35
7	1	7.80	0
Total	45	6.23	1.39

Chart 32 : Serum uric acid distribution for TIMI score in NSTEMI



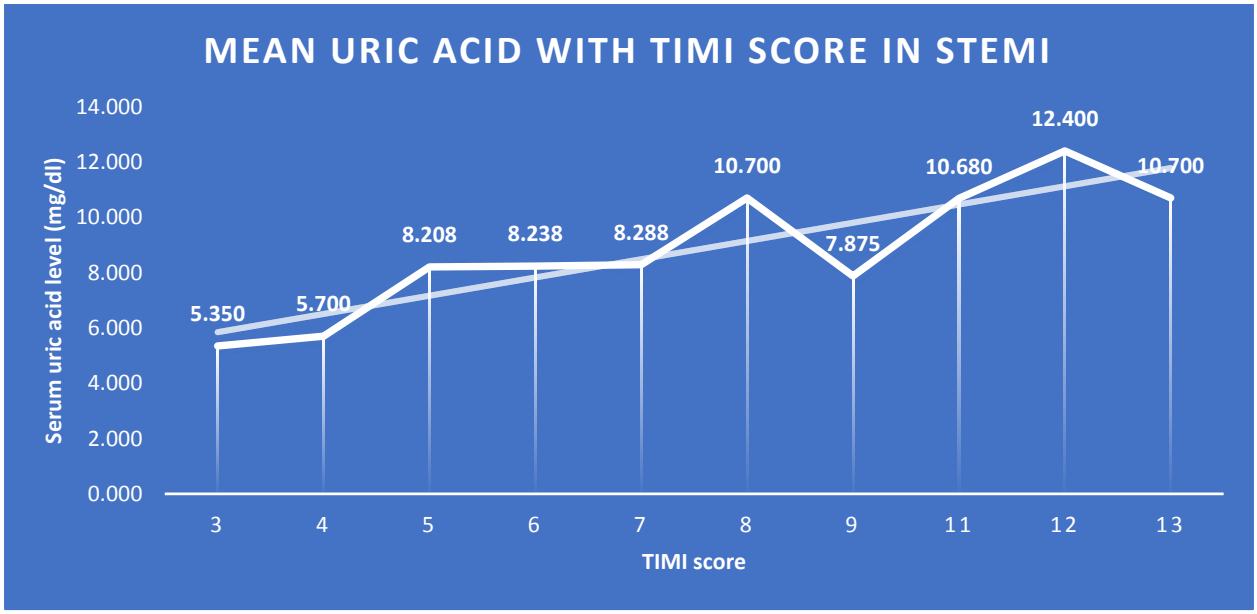
26. MEAN SERUM URIC ACID LEVEL and TIMI score in STEMI

Linear increase in mean serum uric acid is seen in STEMI also

Table 36 : Serum uric acid distribution for TIMI score in STEMI

	Serum uric acid levels (mg/dl)		
TIMI Score	N	Mean	Std. Deviation
3	2	5.35	0.49
4	4	5.70	1.03
5	13	8.20	1.38
6	8	8.23	2.61
7	8	8.28	1.99
8	7	10.70	1.90
9	4	7.87	1.78
11	5	10.68	1.51
12	1	12.40	
13	3	10.70	2.98
Total	55	8.67	2.36

Chart 33 : Serum uric acid distribution for TIMI score in STEMI



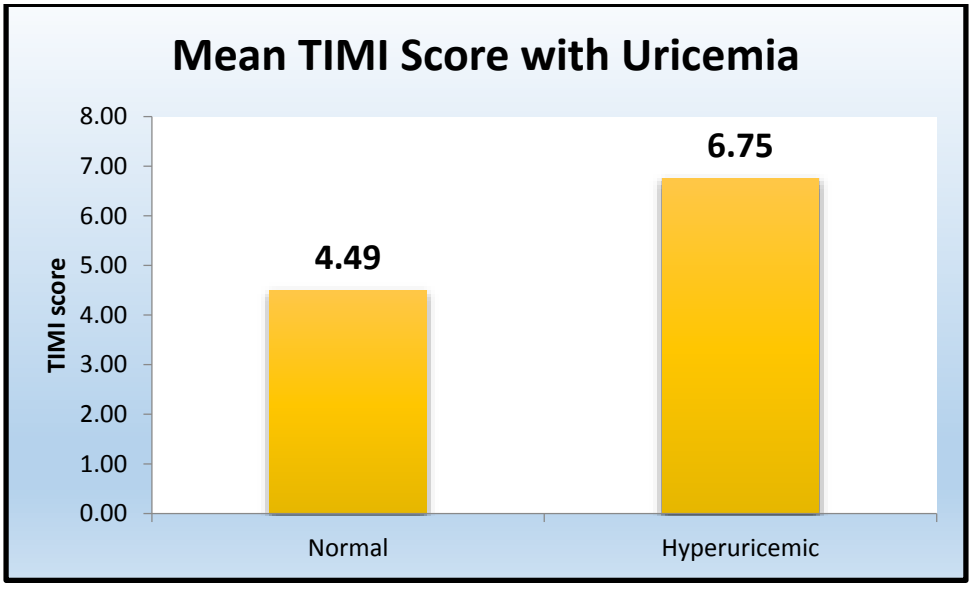
27. TIMI SCORE and HYPERURICEMIA

The mean TIMI score of all hyperuricemic individuals was 6.75 as compared to the sub group with normal serum uric acid levels whose mean TIMI score was 6.75. paired t test was utilized in the statistical analysis and the association is highly significant (p value 0.0005)

Table 37 : Serum uric acid distribution vs TIMI score in general (all MI)

Uric acid status	Number of subjects	Mean TIMI score	Standard Deviation
Normal	41	4.49	1.70
Hyperuricemia	59	6.75	2.48

Chart 34 : Serum uric acid distribution vs TIMI score in general (all MI)



COMPARISON OF TIMI SCORES

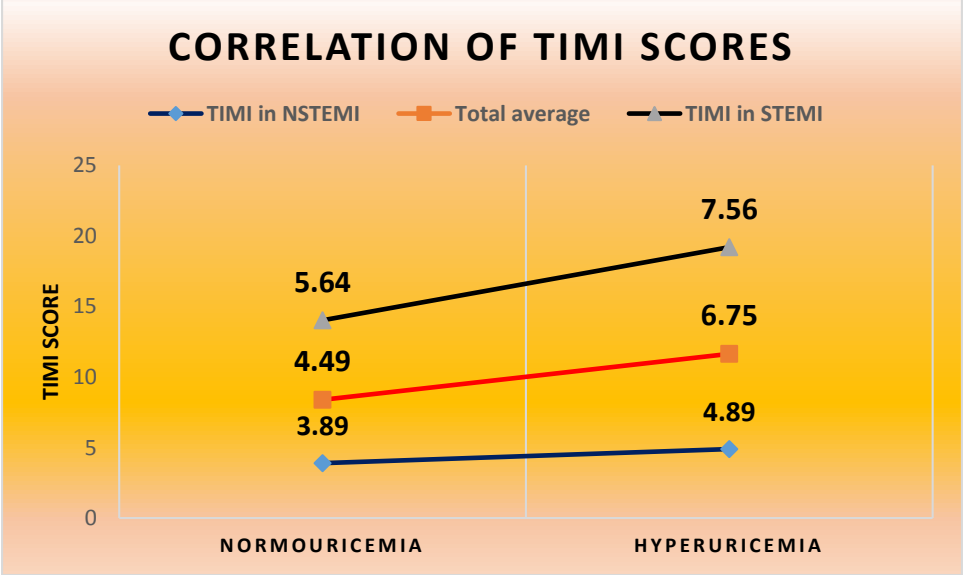
The mean TIMI score are higher in both subgroups of MI (STEMI and NSTEMI) .

The average TIMI score in general is also higher in hyperuricemic subjects.

Table 38: Comparison of TIMI score in hyper and normouremics

	Normouricemia	Hyperuricemia
TIMI in NSTEMI	3.89	4.89
Total average	4.49	6.75
TIMI in STEMI	5.64	7.56

Chart 35: Comparison of TIMI score in hyper and normouricemics



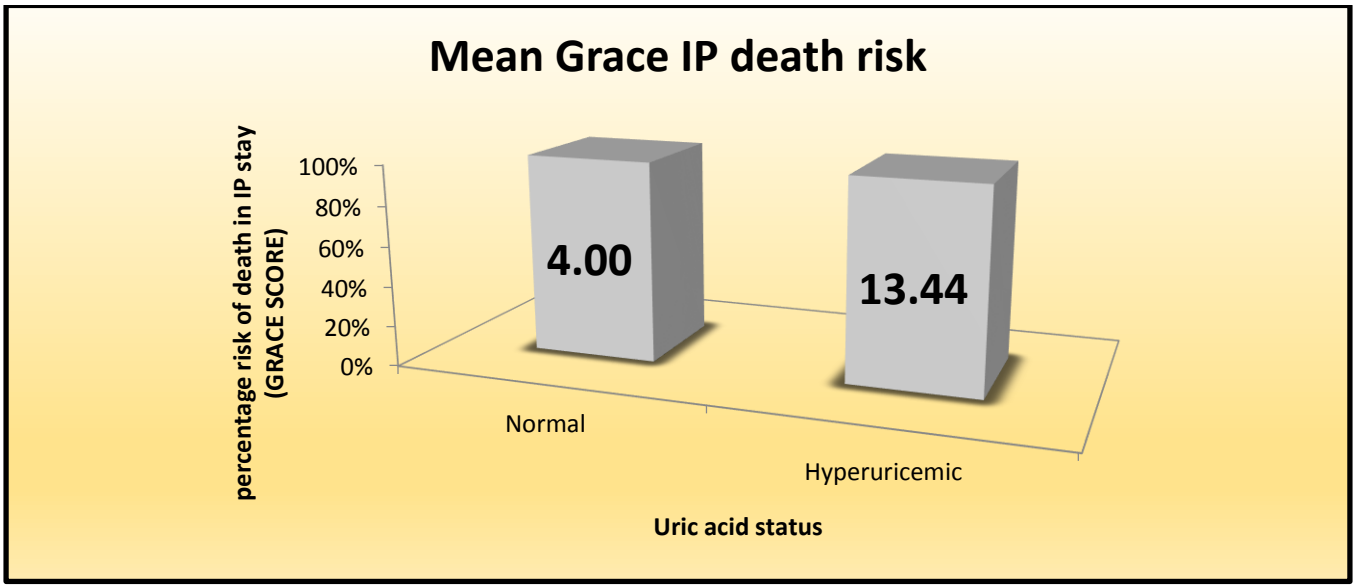
28. GRACE SCORE and SERUM URIC ACID

The grace score was calculated for all patients for their in-hospital risk of mortality. The mean risk of in-hospital mortality in patients with normal uric acid levels (n=41) was 4% whereas it was found to be 13.44% in the 59 subjects with elevated serum uric acid levels. There was a statistically highly significant association between serum uric acid levels and the in hospital risk of mortality as calculated by the GRACE score. (p value 0.0005)

Table 39 : mean GRACE score vs Serum uric acid levels

Serum uric acid status	Number of subjects	Mean GRACE IP risk
NORMAL	41	4.0%
HYPERURICEMIA	59	13.44%

Chart 36 : mean GRACE score vs Serum uric acid levels



25. SERUM URIC ACID and EJECTION FRACTION

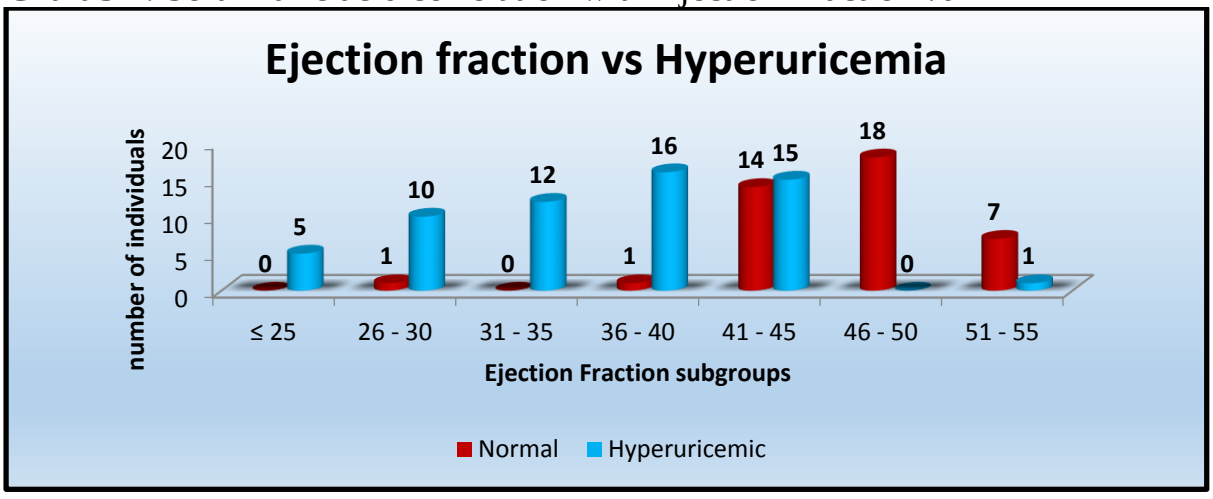
Serum uric acid levels were correlated with the ejection fraction done by 2-D echocardiogram. There was an inverse relationship between serum uric acid levels and the ejection fraction. Higher serum uric acid levels correlated with lower ejection fractions. The result was statistically significant (p value 0.0005)

Table 40 : Serum uric acid correlation with Ejection Fraction %

		Serum uric acid	
		Normal	Hyperuricemic
Ejection Fraction	≤ 25 %	0	5
	26 – 30 %	1	10
	31 – 35 %	0	12
	36 – 40 %	1	16
	41 – 45 %	14	15
	46 – 50 %	18	0
	51 – 55 %	7	1
Total		41	59

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	58.798[a]	6	.0005

Chart 37 : Serum uric acid correlation with Ejection Fraction %



There were 5 subjects in the study population with ejection fraction less than 25%. All patients had serum uric acid more than 9 mg%. All the 11 patients with ejection fraction between 25 – 30% also had serum uric acid more than 9 mg%.

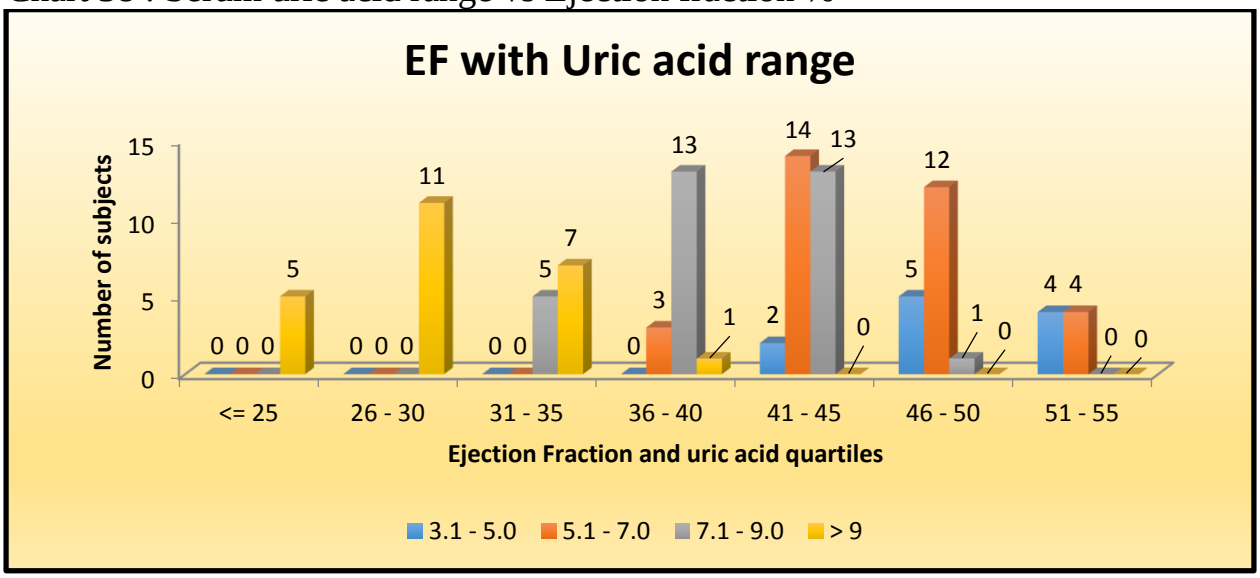
The association is statistically significant (p value 0.0005)

Table 41 : Serum uric acid range vs Ejection fraction %

		Serum uric acid (mg/dl)				Total
		3.1 - 5.0	5.1 - 7.0	7.1 - 9.0	> 9	
Ejection fraction range	<= 25	0	0	0	5	5
	26 - 30	0	0	0	11	11
	31 - 35	0	0	5	7	12
	36 - 40	0	3	13	1	17
	41 - 45	2	14	13	0	29
	46 - 50	5	12	1	0	18
	51 - 55	4	4	0	0	8
Total		11	33	32	24	100

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	124.337[a]	18	.0005

Chart 38 : Serum uric acid range vs Ejection fraction %



DISCUSSION

AGE DISTRIBUTION

The average age of the present study was 57.16 years, which truly reflects the statement that AMI occurs 5-10 years earlier in our population than the western population. The age range varied from 34 years to 80 years. Majority of patients belonged to the age group between 51-60 years, which was also the age group with maximum mortality. However this data was not found to be statistically significant. Study in a Japanese group by M Kuzuya et al showed a decline in uric acid levels between 30-70 years in males, but a rise in uric acid levels after about 45 years in females[75,76].

GENDER DISTRIBUTION

The study included 66% males and 34% females. Male predominance was observed in all the age subgroups included in the study. According to Viola Vaccarino et al, increased early mortality was seen in women after acute myocardial infarction, probably due to their old age; however on controlling the risk factors, females had better survival rates than males in the long run[83,85]. Our study showed no significant association between gender and mortality. Similarly there is no significant association between elevated uric acid levels and male gender, though the mean uric

acid levels were higher in males compared to females. This is in accordance with the studies done by Dharma[86] et al in Indonesia and Nadkar[73] et al.

TROPONIN T AND MORTALITY

Peter Stubbs et al had come to the conclusion that elevated Troponin T in patients with STEMI at the time of admission , increased the risk of subsequent cardiac events as compared to those with normal values[78]. This correlates well with our study, in which 100% of the patients who expired, had elevated Troponin T values and this was found to statistically highly significant.

HYPERURICEMIA AND MORTALITY

The proportion of hyperuricemics in the study population was 59%. Out of the 9 patients who succumbed to death following an acute myocardial infarction, all of them were hyperuricemic at presentation. This establishes a strong significant association between elevated serum uric acid levels and mortality rates in acute coronary syndrome. According to Vladimir Trkulja et al, higher serum uric acid on admission was independently associated with thirty day mortality[67]. The Framingham Heart study which compared serum uric acid with the risk for cardiovascular mortality, established a strong association between baseline serum uric acid levels and coronary artery disease and death. However a causal association

could not be established. Considering the inextricable link with diabetes, hypertension and dyslipidemia, hyperuricemia could be taken as a marker of risk for cardiovascular disease.

ASSOCIATION OF URIC ACID WITH RISK FACTORS

Nadkar et al and Dharma et al could not find any statistically significant association between elevated serum uric acid levels and diabetes mellitus or hypertension. This is in contrast to the LIFE study and NHANES study.

[A] DIABETES MELLITUS AND URIC ACID

42% of the study group were diabetics. No significant association was observed between diabetes mellitus and serum uric acid levels($p=0.119$). D M Cook et al described that uric acid levels were significantly reduced in insulin dependent patients, in those on oral antidiabetic agents as well as non diabetic population with random glucose leves>10 mmol/L,but such a negative association was not seen in our study[80,81].

[B] HYPERTENSION AND URIC ACID

A recent cohort study in subjects with hypertension established a significant association between the two. Our study revealed that the presence of hyperuricemia

in hypertensives was 73%, which has high statistical significance and is in accordance with the cohort study[94].

[C] SMOKING AND URIC ACID

Studies done previously suggest that uric acid levels are low in smokers due to chronic exposure to cigarette smoke, which causes oxidative stress[79]. However significant association was found between smoking and hyperuricemia in this study(p=0.003). The prevalence of hyperuricemia in smokers in our study was found to be 74.47%.

[D} DYSLIPIDEMIA AND URIC ACID

Studies done by Li Chen et al showed a positive correlation between triglyceride level and hyperuricemia[71]. However no statistically significant association could be elicited between dyslipidemia and hyperuricemia in this study. The proportion of hyperuricemics in the dyslipidemic subgroup was 63.6%.

[E] URIC ACID AND PRIOR CEREBROVASCULAR DISEASE

91.67% of patients with a prior history of cerebrovascular event, had elevated serum uric acid levels. The association between the two is statistically significant with a p value of 0.025. According to Ioana Mozos et al, the mortality was higher in stroke patients with hyperuricemia[90]. This association was not seen in our study.

URIC ACID AND HEART BLOCKS

In a study done by Laurens P et al in 158 patients with isotopic pacemaker implantations, he described that the frequency of hyperuricemia is more in such patients[91]. 93.94% of the patients with heart blocks following acute myocardial infarction in our study, were found to be hyperuricemic. Hence significant association exists between heart blocks and hyperuricemia(p=0.003).

URIC ACID AND MI- TYPES AND LOCATIONS

The proportion of STEMI was found to be higher in patients with hyperuricemia than NSTEMI in the study. This association is highly significant. Higher serum uric acid levels were seen in cases of anterior wall and anteroseptal wall MI, when compared to inferior and inferoposterior wall MI. However no association could be established between the location of myocardial infarction and uric acid levels, owing to lesser number of inferior and inferoposterior wall MI cases.

URIC ACID AND TIMI SCORE

The mean TIMI score, which is a prognostication score used for risk stratification, was found to be higher in patients with elevated serum uric acid levels in comparison with those with normal uric acid levels, in both STEMI as well as NSTEMI patients.

There exists a linear relation between the mean serum uric acid levels and TIMI scores.

URIC ACID AND KILLIP CLASS

The mean serum uric acid level has a linear relation with killip class, indicating that serum uric acid levels correlate with the severity of myocardial infarction as assessed by killip classification. 24 patients in the study group had uric acid levels more than 9mg/dl and 91.96% belonged to killip classes 3 and 4. This is a significant association. Similar results were brought out by Trkulja et al and Li Chen et al in their studies, thereby highlighting the prognostic significance of uric acid in myocardial infarction[71].

Mortality in this study was 9% and all the subjects had serum uric acid >9mg/dl. Nadkar et al reported hyperuricemia in 100% of the deaths that occurred in their study[73]. SUA levels > 7mg/dl was the strongest independent predictor of mortality according to Dharma et al.

GRACE SCORE AND URIC ACID

The association between serum uric acid levels and in-hospital risk of mortality, as calculated by GRACE score is highly significant with a p value of 0.0005. Subjects with hyperuricemia had a 9.44% increase in risk of death during hospital stay during

the acute period, which makes SUA a relatively reliable predictor of short term mortality.

URIC ACID AND EJECTION FRACTION

LV dysfunction is an important prognostic indicator in myocardial infarction. In our study, there exists an inverse relation between serum uric acid levels and ejection fraction. 16 subjects in the study population had ejection fraction <30%, all of whom had serum uric acid> 9mg/dl. 66.67% of the subjects that expired during the study period were included in this subgroup. This is further proof that serum uric acid can be used to predict mortality and severity of left ventricular dysfunction and heart failure. This is supported by the study done by Li Chen[71] et al.

CONCLUSIONS

1. Serum uric acid levels are elevated in patients with acute myocardial infarction.

2. There is a strong correlation between serum uric acid levels at the time of admission and in-hospital and short-term mortality in patients with acute myocardial infarction. Patients with elevated SUA levels had higher Killip class in STEMI and higher mortality rates and Major adverse cardiovascular outcomes.

3. Patients with elevated Troponin T had higher mortality.

4. Elevated serum uric acid had positive correlation with systemic hypertension and smoking.

5. Patients with elevated serum uric acid levels had higher TIMI scores and 10% higher risk of in-hospital death as calculated by GRACE score.

6. Patients with elevated serum uric acid had lower ejection fraction during echocardiographic study.

7. Uric acid may be considered as a reliable , noninvasive easily available and cheap independent prognostic marker in predicting the severity of myocardial infarction along with short term outcome.

LIMITATIONS OF THE STUDY

1. The percentage of NSTEMI patients included in the study were more compared to the general statistics as suggested by other landmark studies, which indirectly influenced the mortality rates.
2. The proportion of females included in the study was limited and hence the result cannot be extrapolated into the general population.
3. The follow up period was less than 30 days thereby limiting the study to understanding only the short term outcomes. Long term mortality and morbidity data could not be assessed. Whether serum uric acid could predict long term outcome indicators of mortality and morbidity could not be found out.
4. The study being conducted in a tertiary care center, many of the patients presented as referred cases with a variety of complications of AMI, thereby increasing the number of major adverse cardiac outcomes.

SUMMARY

This study was undertaken to evaluate whether serum uric acid could prove to be a useful marker in predicting the severity of acute myocardial infarction, being a cheap, easily available and simple investigation ,which is crucial for a developing nation like ours. The SUA levels of patients with new onset myocardial infarction were measured and correlated with the severity of involvement using prognostic scores such as Killip, TIMI and GRACE as well as ejection fraction and other complications.. Other co-existing risk factors like diabetes mellitus, systemic hypertension, smoking, dyslipidemia, prior CVA were evaluated for a possible correlation.

In our study of 100 subjects with AMI, 55 had STEMI and 45 had NSTEMI. 8 patients with STEMI and 1 patient with NSTEMI succumbed to death during the study period. Patients with high Troponin T values, high serum uric acid levels had higher mortality rates and belonged to higher Killip class. Positive association was found between hyperuricemia and smoking, hypertension and heart blocks. Out of the patients with uric acid >9mg/dl, 100% had an ejection fraction < 30%, and 91.6% belonged to Killip classes III and IV which was highly significant statistically. Hyperuricemic patients had higher TIMI scores in both STEMI and NSTEMI and also had 9.44% higher risk of in-hospital mortality, as calculated by GRACE score.

High serum uric acid levels correctly predicted the mortality and in-hospital major adverse cardiac events, and proved to be a successful and useful prognostic predictor of short term survival and complications in acute myocardial infarction.

SCOPE FOR FUTURE RESEARCH

Uric acid is an old molecule with new applications. It is an antioxidant which paradoxically has a pro-oxidant action in latter stages of atherosclerosis. Hyperuricemia reduces the production of nitric oxide in vascular endothelium and cause no-reflow during reperfusion. The Xanthine oxidase activity and synthesis of uric acid is disproportionately accelerated in ischaemic conditions. Hence the therapeutic role of inhibiting Xanthine oxidase needs to be studied. Studies have demonstrated uric acid reducing action of Atorvastatin and Losartan. But large trials need to be undertaken to establish a definitive role for these drugs in the future. Some theories claim that uric acid is predominantly released from the necrosed myocardium in AMI, leading to its increased levels. Whether it can serve as a marker of the extent of myocardial necrosis needs to be proven by future studies.

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PROFORMA

NAME :

AGE/SEX :

ADDRESS :

I.P NO: **D.O.A:** **D.O.D:**

COMPLAINTS OF THE PATIENT:

1.CHEST PAIN : YES / NO
2. DURATION OF CHEST PAIN
3. BREATHLESSNESS : YES/ NO
4. PALPITATION : YES/ NO
5. SYNCOPE : YES/ NO
6. SWEATING : YES/ NO

HISTORY IN DETAIL:

HISTORY OF PAST ILLNESS:

CAD	YES/NO
DM	YES/NO
SHTN	YES/NO
FAMILY HISTORY	YES/NO
PRIOR CVA	YES/NO
Usage of Aspirin	YES/NO

PERSONAL HISTORY:

SMOKING AND DURATION:

CLINICAL EXAMINATION :

VITAL SIGNS

BP	PULSE RATE	RESPIRATORY RATE	TEMPERATURE

GENERAL EXAMINATION :

SYSTEMIC EXAMINATION:

1. CARDIOVASCULAR SYSTEM :

2.RESPIRATORY SYSTEM :

3. PER ABDOMEN :

4. CENTRAL NERVOUS SYSTEM :

INVESTIGATIONS :

ECG

RFT S.CREATININE mg/dl
TOTAL CHOLESTEROL mg/dl
S. TAG mg/dl
Random blood sugar mg/dl
TROPONIN **POSITIVE/NEGATIVE**

LOW/HIGH

ECHOCARDIOGRAPHIC FINDINGS:

LVEF %
RV DYSFUNCTION YES/NO
CONCENTRIC LVH YES/NO

	DAY 0	**DAY 3**
S. URIC ACID LEVEL (mg/dl)		

DIAGNOSIS :

DURATION OF HOSPITAL STAY :

FINAL OUTCOME :

SL. NO.	NAME	AGE	SEX	Window Period	Chest Pain	Dyspnea	Others	DM	HTN	Smoking	Family History	CVA	No of Risk Factors	BP	PR	Cholestrol	Troponin	Location of MI	Type of MI	Heart Block	Killip Class	TIMI	GRACE	UA Day 1	UA Day 3	EF	Concentric LVH	RV Dysfunction	Complications	Hospital Stay	Mortality
1	SARASWATHY	77	F	6	Y	N	N	N	Y	N	N	Y	2	HYPER	86	245	LOW	IW	STEMI	N	1	7	4.3	5.4	5.6	50	Y	N	N	5	N
2	CHINNAN	45	M	5	Y	N	Y	Y	N	N	N	N	2	NORMAL	75	232	LOW	AW	STEMI	N	2	6	2.9	4.3	4.1	41	N	N	N	5	N
3	ANBARASI	52	F	4	Y	N	N	Y	N	N	N	N	1	NORMAL	87	182	HIGH	AW	STEMI	N	1	3	2.1	5.7	4.9	53	N	N	N	5	N
4	JEYMUNISHA	55	F	2	Y	Y	Y	Y	Y	N	Y	N	4	HYPER	78	278	HIGH	AS	STEMI	Y	3	5	6.2	9.6	9.3	33	Y	N	LBBB	8	N
5	SATHYANARAYAN	70	M	3	Y	Y	Y	N	Y	Y	N	Y	3	HYPER	77	210	HIGH	AW	NSTEMI	N	2	7	3.3	7.8	7.8	38	Y	N	N	5	N
6	CHINNAKANNAN	70	M	6	Y	Y	N	Y	N	Y	N	N	3	HYPO	106	233	HIGH	AW	STEMI	Y	4	13	50	12.9		34	N	N	qRBBB	2	Y
7	VALLINAYAKI	65	F	2	Y	N	N	N	N	N	N	N	0	NORMAL	86	176	LOW	AW	NSTEMI	N	1	4	3.5	6.2	6.5	54	N	N	N	5	N
8	MUNUSAMY	89	M	2.5	Y	Y	Y	N	Y	Y	N	N	3	HYPER	72	274	HIGH	AS	STEMI	Y	3	7	30	11.2	10.3	27	Y	N	LBBB	8	N
9	ANSARI	46	F	4	Y	N	Y	Y	N	N	Y	N	3	NORMAL	79	342	LOW	IW	NSTEMI	N	1	5	1.1	3	5.4	45	N	N	N	5	N
10	BABU	36	M	4	Y	N	N	Y	N	N	N	N	2	NORMAL	75	302	HIGH	AW	STEMI	N	2	6	1.5	7.8	7.2	42	N	N	N	5	N
11	SHANTHI	45	F	2.5	Y	N	Y	N	Y	N	Y	N	2	HYPER	81	160	LOW	AW	NSTEMI	N	1	3	1.5	3.4	3.3	55	N	N	N	5	N
12	PALANIYAMMAL	55	F	6	Y	N	N	N	Y	N	Y	N	2	HYPER	86	190	LOW	IW	NSTEMI	N	2	4	2.7	7.1	6.4	40	N	N	N	5	N
13	RAVINAMMAL	65	F	5	Y	Y	Y	N	Y	N	N	Y	2	HYPER	89	212	HIGH	AS	NSTEMI	Y	2	6	4.9	7.8	7.8	38	Y	N	LBBB	8	N
14	CHELLAPAPPA	45	F	3	Y	N	N	Y	N	N	N	N	1	NORMAL	92	178	LOW	AS	NSTEMI	N	1	3	1.8	4.5	4.6	55	N	N	N	5	N
15	MARIYAPPAN	52	M	6	Y	N	Y	N	Y	Y	N	N	2	HYPER	70	190	LOW	AW	STEMI	Y	2	5	2.1	8.1	7.8	42	Y	N	LBBB	7	N
16	ESWARAN	45	M	5	Y	N	N	Y	N	N	N	N	2	NORMAL	86	231	HIGH	AW	STEMI	N	1	4	1.6	6.9	6.5	47	N	N	N	5	N
17	BANGARUSAMY	75	M	8	Y	N	Y	Y	N	N	N	N	2	NORMAL	68	199	HIGH	IW	NSTEMI	N	1	5	5.6	7.7	7.1	44	N	N	N	5	N
18	GANESHAN	62	M	9	Y	N	Y	Y	N	N	N	N	1	NORMAL	76	170	LOW	IW	NSTEMI	N	1	4	3	4.1	3.9	47	N	N	N	5	N
19	NAGAMMAL	59	F	5	Y	Y	Y	N	Y	N	Y	Y	4	HYPER	89	222	HIGH	IW	STEMI	N	3	11	60	10.1	9.8	32	Y	N	N	9	Y
20	PARVATHI	56	F	4	Y	N	N	N	Y	N	N	N	1	NORMAL	76	160	LOW	PW+RV	NSTEMI	N	1	3	2.4	4.9	5.1	50	Y	Y	N	5	N
21	RAJESWARAN	68	M	6	Y	N	N	N	Y	Y	Y	N	3	HYPER	77	188	HIGH	AS	STEMI	N	3	8	9.9	8.9	7.1	42	Y	N	N	8	N
22	KANAGAMMAL	78	F	7	Y	N	N	N	Y	N	N	N	2	HYPER	95	210	LOW	AW	STEMI	N	1	9	4.9	5.9	5.1	43	N	N	N	5	N
23	NARAYANAN	68	M	3	Y	Y	Y	N	Y	Y	N	Y	2	HYPER	94	180	HIGH	AW	STEMI	Y	4	11	18	12.1	10.2	18	Y	N	LBBB	12	N
24	PALANIYAMMAL	65	F	8	Y	Y	Y	N	Y	N	N	N	2	HYPO	94	223	HIGH	AW	NSTEMI	N	2	5	34	9.1	9	28	N	N	PERICARDITIS	12	Y
25	DEVAKANNI	70	F	4	N	Y	Y	Y	N	N	N	N	2	NORMAL	96	289	LOW	IW	NSTEMI	Y	2	5	11	7.2	6.5	44	N	N	LBBB	5	N
26	SRINIVASAN	53	M	5	Y	N	Y	N	Y	Y	N	N	2	HYPER	84	170	LOW	AS	STEMI	N	2	6	2.5	7.7	7	41	N	N	N	5	N
27	IYAMMAL	62	F	9	Y	N	Y	Y	Y	N	Y	N	4	HYPER	78	201	HIGH	AS	NSTEMI	N	1	5	1.7	7	7.1	45	Y	N	N	5	N
28	ARULAPPAN	52	M	4	Y	N	N	Y	N	N	N	N	1	NORMAL	84	190	LOW	AW	NSTEMI	N	1	3	2	4.1	3.9	51	N	N	N	5	N
29	KATHURAMALAI	52	M	6	Y	N	Y	Y	Y	Y	N	N	4	HYPER	83	245	HIGH	IW	STEMI	Y	2	5	2.8	8.9	9.4	38	Y	N	RBBB	7	N
30	NATARAJ	69	M	7	Y	Y	N	N	Y	Y	Y	N	3	HYPO	91	189	HIGH	IW+PW+R	STEMI	Y	4	12	78	12.4	12.2	22	Y	Y	CHB	3	Y

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31	SHAJAHAN	41	M	4	Y	Y	Y	N	Y	Y	N	N	3	HYPER	76	216	HIGH	AW	NSTEMI	N	2	5	2.3	8.5	7.2	44	N	N	N	5	N
32	TAMILSEVAN	70	M	6	Y	N	Y	N	N	Y	N	N	2	NORMAL	77	199	LOW	AW	NSTEMI	N	1	5	4.9	5.5	5.2	48	N	N	N	5	N
33	ANBARASI	44	F	4	Y	N	N	Y	N	N	N	N	2	NORMAL	70	234	LOW	AW	STEMI	N	1	3	1.1	5	4.9	50	N	N	N	5	N
34	ARJUNAN	55	M	5	Y	N	N	Y	N	N	Y	N	2	HYPO	87	177	HIGH	IW	STEMI	N	1	4	13	4.5	4.3	55	N	N	N	5	N
35	BALAKRISHNAN	46	M	3	Y	Y	Y	Y	N	N	N	N	1	HYPO	88	190	LOW	IW+PW	STEMI	Y	3	6	29	10.8	10.5	33	Y	N	LBBB	10	N
36	MALAR	51	F	5	Y	N	Y	N	Y	N	N	N	2	HYPER	88	245	HIGH	AW	STEMI	N	2	6	2.8	6.5	6	39	N	N	N	5	N
37	PALANIMUTHU	78	M	4	Y	N	Y	N	Y	Y	N	N	3	HYPER	96	240	LOW	AW	STEMI	N	2	13	9.5	7.3	7	35	Y	N	N	5	N
38	LOGANATHAN	58	M	5	Y	Y	N	N	Y	Y	N	N	3	HYPO	94	221	HIGH	AW	STEMI	Y	3	11	48	9.9		27	Y	Y	CHB+VSR	1*	Y
39	SITHAN	60	M	8	Y	N	N	N	Y	Y	N	N	2	HYPER	92	179	HIGH	AS	NSTEMI	N	2	4	3.8	7.8	5.2	40	Y	N	N	5	N
40	CHINNAPAMANI	62	M	4	N	N	Y	Y	N	N	N	N	2	NORMAL	83	226	HIGH	AS	NSTEMI	N	1	4	3.5	6.5	6	46	N	N	N	5	N
41	SELVAM	42	M	1	Y	N	N	N	Y	Y	Y	N	4	HYPER	75	270	LOW	AW	STEMI	Y	2	6	6.2	8.4	6.9	40	N	N	LBBB	5	N
42	PURMANGATHAN	65	M	7	Y	Y	N	N	Y	Y	N	N	3	NORMAL	86	199	HIGH	AW	STEMI	N	3	8	16	10	10.8	30	Y	N	N	7	Y
43	PERIYANNAN	68	M	5	Y	N	Y	N	Y	Y	N	N	2	HYPER	84	160	LOW	IW	NSTEMI	N	1	5	2.5	5.6	5.5	48	Y	N	N	5	N
44	MADHAIYAN	53	M	5	Y	N	Y	N	Y	Y	Y	N	3	HYPER	73	180	LOW	IW	NSTEMI	N	1	4	1.1	5.2	5	50	N	N	N	5	N
45	KRISHNAN	45	M	3	Y	N	N	N	Y	Y	Y	N	4	HYPER	76	256	LOW	AS	STEMI	N	1	4	1	5.3	4.9	54	N	N	N	5	N
46	PALANIYAMMAL	65	F	8	Y	N	N	N	Y	N	N	N	2	HYPER	87	227	HIGH	AW	STEMI	N	2	7	5.8	7.8	8.3	43	N	N	N	5	N
47	ANGUMANI	61	F	6	Y	Y	Y	Y	N	N	N	Y	2	NORMAL	82	212	HIGH	AW	NSTEMI	N	3	5	7.7	9.1	9	35	Y	N	N	8	N
48	SENTHILKUMAR	47	M	4	Y	Y	Y	N	Y	Y	N	N	3	HYPER	110	267	HIGH	AW	STEMI	N	4	8	16	12.8	12.7	20	Y	N	N	10	N
49	CHINNAPONNU	80	F	7	Y	Y	Y	Y	N	N	Y	Y	3	HYPER	80	210	HIGH	AW	STEMI	N	4	11	43	11.9	12.4	17	Y	N	VT	10	Y
50	MADESHWARAN	54	M	3	Y	N	Y	N	Y	Y	N	N	2	HYPER	100	190	LOW	IW	NSTEMI	N	1	3	1.7	3.9	4.2	50	N	N	N	5	N
51	BALAMURUGAN	50	M	5	Y	N	N	Y	N	N	N	N	2	NORMAL	90	290	LOW	IW	NSTEMI	N	1	4	2.1	4.5	5.1	45	N	N	N	5	N
52	PRAKASH	40	M	5	Y	N	N	N	Y	Y	N	N	3	HYPER	110	210	HIGH	AW	STEMI	N	2	8	2.4	7.9	7.5	35	Y	N	N	5	N
53	ALLIMUTHU	55	M	10	Y	N	Y	Y	N	N	N	N	1	NORMAL	90	159	LOW	AW	NSTEMI	N	2	4	5.2	7	6.9	40	N	N	N	5	N
54	SUBRAMANI	67	M	4	Y	Y	N	N	N	Y	N	Y	1	NORMAL	110	187	HIGH	AW	STEMI	N	3	9	25	7.9	8	34	N	N	N	7	N
55	ALAMELU	50	F	6	Y	N	Y	Y	N	N	Y	N	2	NORMAL	89	190	LOW	IW	NSTEMI	N	1	4	1.9	5.5	5.1	44	N	N	N	5	N
56	MANICKAM	65	M	3	Y	Y	Y	N	Y	Y	N	N	2	HYPO	69	166	HIGH	AS	STEMI	Y	3	11	19	8.9	7.8	37	Y	N	LBBB	9	N
57	ANJALAI	60	F	6	Y	N	N	Y	N	N	N	N	2	NORMAL	73	230	LOW	AS	NSTEMI	N	2	4	5.7	4.3	5	43	N	N	N	5	N
58	ELUMALAI	35	M	5	Y	N	N	Y	N	N	N	N	2	NORMAL	75	201	HIGH	AS	NSTEMI	N	1	4	0.8	5.9	5.3	47	N	N	N	5	N
59	VENGATESWARI	55	F	2	Y	N	N	N	N	N	Y	N	1	NORMAL	78	190	LOW	AW	NSTEMI	N	1	4	2.3	6.7	6.9	45	N	N	N	5	N
60	RAJENDRAN	55	M	2	Y	N	N	N	Y	Y	N	N	3	HYPER	98	245	HIGH	AS	STEMI	N	2	7	3.2	7.9	8	44	N	N	N	5	N
61	DHANAM	60	F	1	Y	N	N	Y	N	N	N	N	2	NORMAL	79	267	LOW	IW	STEMI	N	1	4	2.7	5.2	6.1	45	N	N	N	5	N
62	GURUNADHAN	72	M	4	Y	Y	Y	Y	Y	Y	Y	N	5	HYPO	120	290	HIGH	IW+PW+RV	STEMI	N	4	13	85	11.9	11.8	26	Y	Y	N	12	N

63	SHAKILA BANU	34	F	4	Y	N	Y	N	Y	N	N	N	2	HYPER	98	210	LOW	AW	STEMI	N	1	5	0.6	4.9	5.8	44	N	N	N	5	N
64	SUNDARARAJAN	47	M	2	Y	N	Y	N	N	Y	N	N	1	NORMAL	82	197	HIGH	AW	STEMI	N	2	5	3.8	7.6	7.1	38	N	N	N	5	N
65	CHINNU	49	M	3	Y	N	N	Y	N	N	N	N	2	NORMAL	81	230	LOW	AW	NSTEMI	N	1	3	1.9	5.5	5.8	49	N	N	N	5	N
66	PATHEELA	47	F	5	Y	Y	Y	N	Y	N	Y	N	3	HYPER	74	265	HIGH	AS	STEMI	Y	4	6	6.7	12.6	12.9	28	Y	N	LBBB	12	N
67	AMANULLAH	43	M	1	Y	N	Y	Y	N	N	N	N	1	NORMAL	83	189	LOW	IW	NSTEMI	N	1	4	1.3	6.1	5.4	48	N	N	N	5	N
68	VARADHAMMAL	60	F	4	Y	N	N	N	N	N	Y	Y	2	NORMAL	87	230	LOW	IW	STEMI	N	2	5	6.2	7.2	6.9	42	N	N	N	5	N
69	THANGAVEL	65	M	4	Y	N	N	N	N	Y	Y	N	2	NORMAL	91	167	HIGH	AS	STEMI	N	1	7	4.5	5.7	6.2	45	N	N	N	5	N
70	RAJU	60	M	3.5	Y	Y	N	N	Y	Y	N	N	3	HYPER	73	296	HIGH	AW	STEMI	N	3	5	6.7	8.6	8.8	34	Y	N	N	8	N
71	SUBRAMANI	54	M	2	Y	Y	Y	N	N	Y	N	N	2	NORMAL	84	211	HIGH	AS	STEMI	N	3	5	8.7	9.9	9.2	30	N	N	N	8	N
72	BABU	53	M	3	Y	N	N	Y	N	N	N	N	1	NORMAL	75	130	LOW	IW	NSTEMI	N	1	4	2	6.4	5.8	43	N	N	N	5	N
73	PREMA	58	F	5	Y	N	Y	N	Y	N	N	N	2	NORMAL	79	278	HIGH	AW	NSTEMI	N	2	4	5.2	6.9	5.2	41	N	N	N	5	N
74	SOLAI	59	M	3	Y	N	Y	N	Y	Y	Y	N	4	HYPER	87	266	HIGH	AS	STEMI	N	2	6	4.3	7.5	7.4	42	Y	N	N	5	N
75	MANICKAM	65	M	2	Y	N	Y	N	Y	Y	N	N	3	HYPER	94	284	LOW	AW	STEMI	N	1	7	3.5	7.3	7	47	Y	N	N	5	N
76	PAPPATHI	45	F	2.5	Y	N	Y	N	Y	N	Y	N	2	HYPER	78	186	HIGH	AS	NSTEMI	N	1	3	0.8	4.9	5.3	49	N	N	N	5	N
77	SARAVANAN	49	M	6	Y	Y	N	N	Y	Y	Y	N	4	HYPER	104	289	HIGH	AS	STEMI	Y	3	8	16.6	9.8	9.1	30	N	N	LBBB+VT	3*	Y
78	ALAMELU	75	F	4	Y	N	N	Y	N	N	Y	N	3	NORMAL	74	210	HIGH	IW	STEMI	N	2	9	14	7.4	7.2	40	N	N	N	5	N
79	SUKKARAIYAMMAL	45	F	3	Y	Y	N	N	N	N	Y	N	1	NORMAL	77	177	LOW	AW	NSTEMI	N	1	3	1.5	4.2	4	50	N	N	N	5	N
80	PERUMAL	57	M	2.5	Y	Y	Y	N	Y	Y	N	N	3	HYPER	96	263	HIGH	AS	STEMI	N	3	7	8.6	8.9	8.7	33	Y	N	N	9	N
81	SYED AMEER	52	M	2	Y	N	Y	N	N	Y	N	N	2	NORMAL	85	245	LOW	AS	NSTEMI	N	1	3	2.1	5.3	5.8	55	N	N	N	5	N
82	THIYAGARAJAN	62	M	4	Y	Y	Y	N	N	Y	N	N	1	NORMAL	84	185	HIGH	AW	STEMI	N	3	5	13	9.6	9.2	34	N	N	N	8	N
83	IYADURAI	60	M	3	N	N	Y	Y	Y	Y	Y	Y	5	HYPER	76	201	HIGH	AW	NSTEMI	N	2	5	3.2	7.8	7	40	Y	N	N	5	N
84	GNANAMMAL	57	F	5	Y	N	Y	Y	N	N	Y	N	2	NORMAL	79	168	LOW	IW	STEMI	N	2	5	4.6	6.5	6	44	N	N	N	5	N
85	SELVARAJ	50	M	3	Y	N	Y	N	Y	Y	Y	N	3	HYPER	82	196	HIGH	IW	NSTEMI	N	1	3	1.1	5.8	5.4	48	Y	N	N	5	N
86	CHINNAPONNU	40	F	5	Y	Y	N	Y	N	N	Y	N	3	NORMAL	89	231	LOW	IW	NSTEMI	N	2	5	2.5	6.9	5.2	42	N	N	N	5	N
87	GOVINDHARAJ	40	M	4	Y	N	N	Y	Y	N	Y	N	4	HYPER	76	230	LOW	AW	STEMI	N	2	5	1.2	7.1	7.3	40	N	N	N	5	N
88	PALANIYAPPAN	68	M	4.5	Y	Y	Y	N	Y	Y	Y	N	4	HYPER	72	213	HIGH	AS	STEMI	N	4	8	22	11.8	12.3	26	Y	N	N	14	N
89	VEERAMMAL	72	F	3	Y	N	Y	N	N	N	Y	N	1	NORMAL	85	176	LOW	AS	NSTEMI	N	1	5	5.9	5.8	5	41	N	N	N	5	N
90	GOPAL	75	M	2	Y	N	Y	Y	Y	N	Y	N	4	HYPER	87	256	HIGH	AW	NSTEMI	N	2	6	7.5	6.8	7.4	39	N	N	N	5	N
91	RAMESH BABU	52	M	4	Y	Y	Y	N	Y	Y	N	N	3	HYPER	89	267	HIGH	AS	STEMI	N	3	5	5.4	9.7	8.1	30	Y	N	N	9	N
92	JAGADEESAN	56	M	3	Y	Y	N	Y	Y	Y	Y	N	5	HYPER	98	204	HIGH	AW	STEMI	N	3	7	12	10.4	10.8	33	Y	N	N	3*	Y
93	ARUNACHALAM	65	M	8	Y	N	N	Y	N	N	N	N	1	NORMAL	90	158	LOW	IW	NSTEMI	N	1	5	4.5	5.6	5.4	40	N	N	N	5	N
94	NARASAPPAN	54	M	6	Y	N	Y	N	Y	Y	N	N	3	HYPER	77	234	LOW	AS	NSTEMI	N	1	5	5.9	6.2	6.6	45	N	N	N	5	N
95	CHINNASAMY	50	M	5	Y	N	N	Y	N	N	N	N	1	NORMAL	84	164	HIGH	IW	NSTEMI	N	2	4	3.7	7.9	7.3	40	N	N	N	5	N

96	KANDHAN	56	M	2.5	Y	N	N	Y	Y	Y	Y	Y	5	HYPER	83	257	LOW	AW	NSTEMI	N	1	6	1.5	6.9	7.1	42	Y	N	N	5	N
97	JAGADEESAN	52	M	7	Y	N	Y	Y	Y	Y	N	N	2	HYPER	79	167	HIGH	AW	STEMI	N	2	5	2.7	7.2	7	40	N	N	N	5	N
98	GOVINDHRAJ	77	M	6	Y	Y	N	Y	Y	Y	N	Y	3	HYPER	83	183	HIGH	AS	STEMI	N	3	9	19	10.2	10.2	30	N	N	N	8	N
99	MASJAN	43	M	5	Y	Y	N	N	Y	Y	N	N	3	HYPO	78	218	LOW	AW	STEMI	N	4	8	9.3	11.9	12.4	17	Y	N	N	10	N
100	MADHU	60	M	4	Y	N	Y	N	Y	Y	Y	N	3	HYPER	90	148	LOW	IW	NSTEMI	N	2	4	3.8	4.1	4.3	48	N	N	N	5	N